AUSCULTATION OF THE HEART *

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HEART sounds and murmurs have been recorded with electronic apparatus in which the lower frequencies or pitches have been severely attenuated or filtered, resembling the effect of the human hearing mechanism and stethoscope (Rappaport and Sprague 1942, Leatham 1949, 1952). Graphic records have been made simultaneously from different areas together with pressure pulses from the heart and great vessels and the electrocardiogram. The records can be used to increase the accuracy of clinical auscultation; the improvement is mainly in appreciating the timing and relation to each other of heart sounds and murmurs rather than in any increase in perception of faint murmurs, for here phonocardiography does not compete advantageously with the remarkable sensitivity and selectivity of the human ear.

Phonocardiograms of the sort described, containing mainly the higher frequencies, were first used to obtain correlation with clinical auscultation; but these high-frequency recordings have also proved the most valuable in relating heart sounds and murmurs to hæmodynamics, especially when the graphs are taken simultaneously from at least two different areas. This technique has established the important principle that there is an asynchrony between left and right ventricles which must be taken into account for any accurate analysis of heart sounds and murmurs. It is much easier technically to obtain phonocardiograms containing more low-frequency vibrations than can be heard, but so far analysis of these records has yielded disappointing and confusing results and will not be discussed except in the study of triple rhythm.

HEART SOUNDS

Heart sounds comprise:

Valve-closure sounds (first and second heart sounds).
Atrioventricular-valve opening sounds (opening snap of mitral and tricuspid valves).
Ejection sounds (aortic and pulmonary).
Ventricular filling sounds (triple rhythm).
Extracardiac sounds.

Valve-closure Sounds

It is generally accepted that the major components of the first sound are due to closure of the mitral and tricuspid valves at the onset of the rise of pressure in the ventricles, and that the second sound is due to closure of the aortic and pulmonary valves when the pressure in the ventricles has fallen below that in the great vessels. Each sound is, therefore, composed of both left and right sided components, which must be separated or split for accurate analysis.

FIRST HEART SOUNDS

At the lower end of the sternum in healthy subjects clinicians commonly hear close splitting of the first sound into two major components. This is almost certainly due to asynchronous closure of the mitral and tricuspid valves. That the mitral valve shuts first is suggested by the relatively greater intensity of the first component at the mitral area, and of the second at the tricuspid area. This precedence of left-sided events (which holds true for the second sound also) is supported by the relation of the first component to ejection into the aorta as shown by the carotid pulse (see fig. 1 of Leatham 1954), and has been confirmed by electrokymographic studies (Reinhold and Rudhe 1957). The splitting is best heard at the lower end of the sternum, probably because this site is nearest to the relatively softer tricuspid component which may not be well transmitted to the mitral area and the interval separating the two components is narrow (0·02–0·03 sec. between onsets). The importance of splitting of the first sound lies in its differentiation from an early systolic ejection sound, an atrial sound, and an atrial systolic (presystolic) murmur (to be discussed later). Briefly, the ejection sound is normally maximal at the base, the atrial sound is much lower in pitch, and the atrial systolic murmur is maximal at the apex after exertion and is almost invariably accompanied by the other signs of mitral stenosis such as the opening snap and a mitral diastolic murmur.

The tricuspid component of the first sound is abnormally delayed in complete right bundle-branch block owing to delay in onset of rise of pressure in the right ventricle (Leatham and Gray 1956). Wide splitting of the first heart sound at the lower end of the sternum, especially when accompanied by wide splitting of the second sound at the pulmonary area, is diagnostic of this electrocardiographic abnormality (see fig. 2 of Leatham 1954). There is no alteration in the first or second sounds associated with the presence of an rSR complex or so-called incomplete right bundle-branch block, for there is no delay in rise of pressure in the right ventricle in these cases (Leatham and Gray 1956). Abnormal splitting of the *first* sound is not a feature of left bundle-branch block, even when complete; and this has been explained by the demonstration of absence of delay in the *onset* of contraction of the left ventricle (Braunwald and Morrow 1956). The auscultatory diagnosis of left bundle-branch block, however, can be made from the second sound (discussed later).

The mitral component of the first sound is abnormally delayed in mitral stenosis probably because the left ventricular pressure has to rise higher than normal before exceeding the raised left atrial pressure and shutting the valve. As a result the order of valve closure may be reversed, mitral after tricuspid (fig. 11); and this is responsible for the well-known delay in the loud components of the first sound in mitral stenosis (Weiss and Joachim 1911, Cossio and Berconsky 1943, Wells 1954, Julian and Davies 1957), but this is not an auscultatory sign.

The intensity of the first sound seems to be governed mainly by the position of the atrioventricular valve cusps at the onset of ventricular systole. The first sound is loud if, at the beginning of ventricular systole, the valves are wide open from continuation of flow of blood from atria to ventricles, and therefore have a long way to shut. This may be due to prolongation of ventricular filling from atrioventricular valve stenosis or increased atrioventricular flow from high cardiac output or left-to-right shunt, or to shortening of atrioventricular filling time (diastole) from tachycardia, or to a late surge of filling

* The first Goulstonian lecture for 1958, delivered at the Royal College of Physicians of London on Jan. 14.

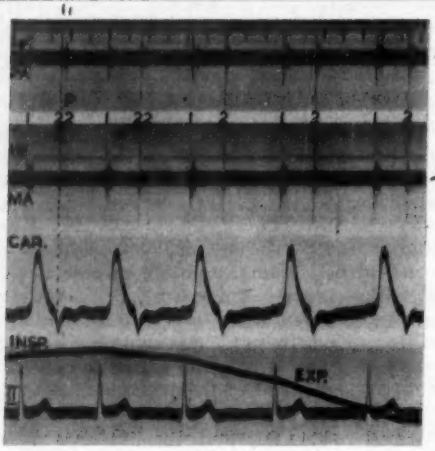

Fig. 1—Normal subject.

Simultaneous high frequency (H.F.) phonocardiograms from the pulmonary (P.A.) and mitral (M.A.) areas, indirect carotid arterial tracing (CAR), and electrocardiogram. During inspiration (insp.) the second sound (2) in the pulmonary area is split by 0·05 sec. and becomes single in the expiratory phase of respiration. The first component is shown to be aortic (A) by its synchrony with the dicrotic notch of the carotid tracing, and the second pulmonary (P) by its localisation near the pulmonary area, for it is too soft to be transmitted to the mitral area. It follows that the second sound in the mitral area is due solely to aortic closure, and in the pulmonary area to both aortic and pulmonary closure either fused or separate. Time intervals in this and subsequent records are 0·20 and 0·04 sec.

from atrial contraction close to ventricular contraction (short P-R interval [Wolferth and Margolies 1930]).* A varying relation between atrial and ventricular contraction, as in complete heart-block, produces varying intensity of the first heart sound. Diminished intensity of the first sound may be due to these factors in reverse or, much more commonly, to poor conduction of heart sounds because of emphysema or a thick chest wall. Changes in the rate of contraction of ventricular muscle may prove to be yet another factor.

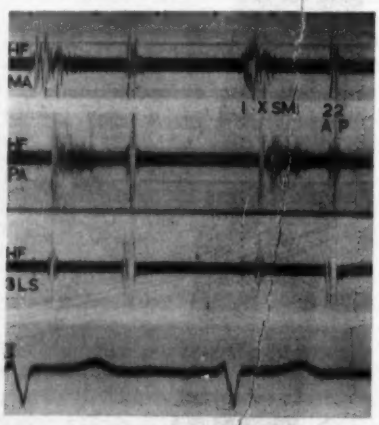

Fig. 2—Pulmonary hypertension (ventricular septal defect with right-to-left shunt).

Accentuation of pulmonary component of second sound which appears to drown the aortic component on auscultation at the pulmonary area and is transmitted to the mitral area where the splitting can be detected because the two components are more equal in intensity. The greatly dilated pulmonary artery causes an ejection sound (X) and systolic murmur (S.M.).

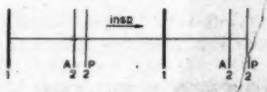

Fig. 3—Wide splitting of second sound in expiration.

Early aortic component (mitral regurgitation). Delayed pulmonary component (delayed activation of right ventricle from complete right bundle-branch block; increased stroke volume of right ventricle; pulmonary stenosis). Further increase in splitting on inspiration in most cases.

SECOND HEART SOUND

Analysis of the second heart sound is impossible without appreciating that in the pulmonary area it consists of both aortic and pulmonary components. Splitting of the second heart sound in the pulmonary area during inspiration into an earlier aortic component and a later pulmonary (fig. 1) can be readily detected in most children and young adults and many older subjects: it is mainly due to delay in pulmonary closure, probably from the transient inspiratory increase in stroke volume of the right ventricle without a similar increase of the left

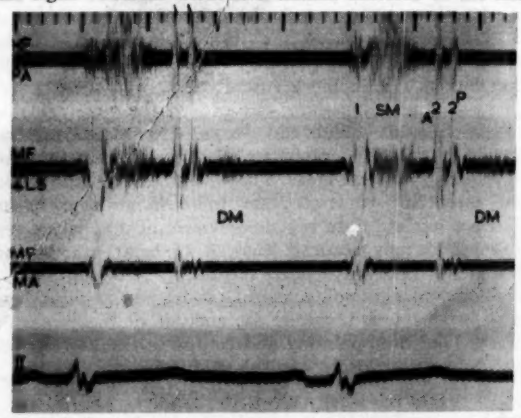

Fig. 4—Atrial septal defect with normal pulmonary pressures and left-to-right shunt.

Splitting of the second sound is abnormally wide (0·04–0·05 sec.) in the expiratory phase of respiration with little further increase on inspiration. The pulmonary component of the second sound is not accentuated from pulmonary hypertension but may be transmitted to the apex because this is formed by the right ventricle. The pulmonary ejection murmur (S.M.) is of no more than moderate intensity and is rather early in systole, finishing long before both components of the second sound so that the splitting is an obvious physical sign. The increased right-sided flow is thought to be responsible for all these signs and for the soft tricuspid diastolic murmur (D.M.) shown in the medium frequency recording (M.F.) from the fourth left space (4 L.S.).

(Leatham and Towers 1951, Leatham 1954). The splitting spreads to the left parasternal area, and sometimes to the aortic area, but not to the mitral area (unless a dilated right ventricle forms the apex) where the second sound is normally single and is due solely to aortic closure. The relative softness of pulmonary closure is responsible for its localisation around the pulmonary area. Only an abnormally loud pulmonary closure sound from pulmonary hypertension is transmitted to the apex (unless this is formed by the right ventricle), and splitting of the second sound at the apex is an excellent sign of pulmonary hypertension (fig. 2). If the second sound cannot be analysed properly by separation into its components, it is still worth stating whether the total second

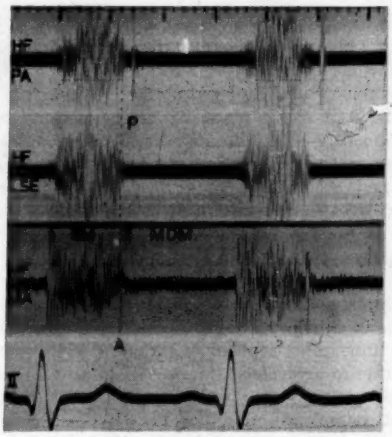

Fig. 5—Ventricular septal defect with normal pulmonary pressures and left-to-right shunt.

Splitting of the second sound is not obvious clinically because the aortic component is drowned in the pansystolic murmur. The splitting is a little wider than normal, owing to shortening of left ventricular systole from diminished resistance to left ventricular outflow, since the stroke volumes of the two ventricles are equally increased. The mitral diastolic murmur (M.D.M.) is due to increased flow through the mitral valve.

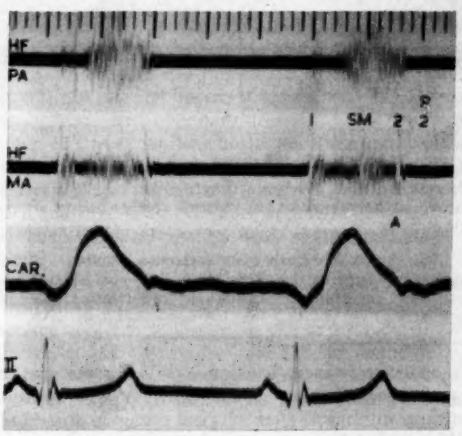

Fig. 6—Pure pulmonary stenosis (moderate severity).

Pulmonary closure is soft and greatly delayed (0·09 sec.) producing wide splitting of the second sound. With severe stenosis it may be impossible to detect the splitting clinically because the loud systolic murmur drowns aortic closure in the pulmonary area, and pulmonary closure is soft or absent. The pulmonary systolic murmur is of ejection pattern finishing well before pulmonary closure. Aortic closure is identified by the simultaneous phonocardiogram from the mitral area, and by its synchrony with the dicrotic notch of the carotid tracing.

sound in the pulmonary area is louder than in the aortic area. This happens frequently in severe pulmonary hypertension, probably in main because the louder and later pulmonary component drowns the earlier aortic component (fig. 2). In these cases, however, the splitting can usually be detected in the mitral area where the two components are more equal in intensity.

A great deal of information can be obtained by carefully noting the behaviour of the second sound during respiration. Inspiration in normal subjects produces delay in pulmonary closure, which may even exceed 0·08 sec. The point to note, however, is that aortic and pulmonary components are normally almost superimposed in the expiratory phase of continued respiration (fig. 1), which is the very time therefore to listen for abnormal splitting.

Abnormally wide splitting of the second sound in the expiratory phase of respiration with aortic closure preceding pulmonary (shown usually by a further increase in width of splitting on inspiration) may be caused by early closure of the aortic valve due to diminished resistance to left ventricular ejection as in mitral regurgitation, but is more commonly caused by abnormal delay in pulmonary closure. This may be due to delay in electrical activation of the right ventricle from complete right bundle-branch block, or to selective increase in stroke volume of the right ventricle due to a left-to-right shunt at atrial level (atrial septal defect or anomalous pulmonary venous return) or to pulmonary stenosis (fig. 3). It is uncertain whether the delay in pulmonary closure accompanying left-to-right shunts is due directly to prolongation of right ventricular ejection from the increased-stroke volume or indirectly to abnormally low

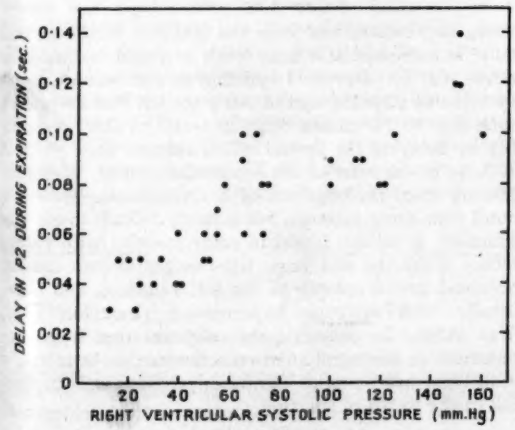

Fig. 7—Pulmonary stenosis.

Relation of delay in pulmonary closure (when recorded, and as shown by the width of splitting of second sound) to the severity of the pulmonary stenosis (right ventricular systolic pressure).

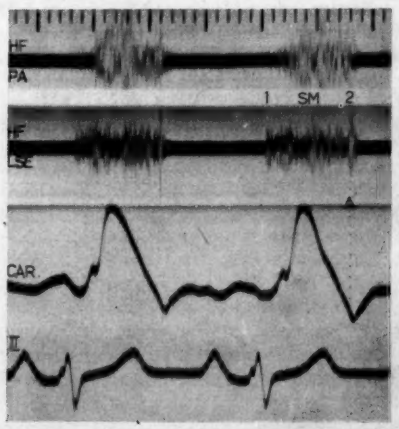

Fig. 8—Pulmonary stenosis with ventricular septal defect and right-to-left shunt (cyanotic Fallot's tetralogy).

Greater reduction in pulmonary flow than in pure pulmonary stenosis, and no late pulmonary closure can be recorded. The single second sound is due to aortic closure as shown by the carotid tracing.

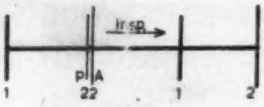

Fig. 9

Fig. 12

Fig. 9—Reversed splitting of second sound.
Delayed activation of left ventricle from left bundle-branch block; increased stroke volume of left ventricle (patent ductus arteriosus); aortic stenosis.

Fig. 12—Early systolic ejection sounds.
Pulmonary: hypertension from any cause; valve stenosis. Aortic: coarctation; aneurysm or dilatation; hypertension; stenosis or regurgitation.

pulmonary resistance (Jonsson 1958). Against the theory of prolonged ejection is the delay of the splitting in returning to normal after surgical repair in some cases of atrial septal defect. Against the resistance theory is the fact that many patients with high pulmonary resistance have normal splitting of the second sound. In atrial septal defect (fig. 4) the splitting tends to be wide (Barber et al. 1950) and fixed with little further increase on inspiration (Leatham and Gray 1956), presumably because the right ventricle is already fully loaded by the shunt. Wide fixed splitting of the second sound (by 0·04–0·05 sec.) has proved a most useful sign of atrial septal defect and is very readily detected because the systolic murmur ceases well before both components of the second sound; it also indicates that the main shunt is from left to right. With reversal of the shunt from pulmonary hypertension the splitting narrows or disappears, and this is a useful clinical indication that the case is inoperable. In ventricular septal defect with left-to-right shunt splitting of the second sound does not attract attention but may be a little wider than normal (fig. 5), perhaps owing to shortening of left ventricular systole rather than to increased stroke volume since *both* ventricles are overloaded; this is a difficult physical sign to detect because the pansystolic murmur tends to drown aortic closure. The greatest prolongation of right ventricular systole takes place in pulmonary stenosis (fig. 6) and is roughly proportional to the degree of stenosis (Leatham and Weitzman 1957). If the late soft pulmonary closure vibration can be recorded (as it can in 85% of cases of pulmonary stenosis with normal aortic root), the time interval between aortic and pulmonary closure can

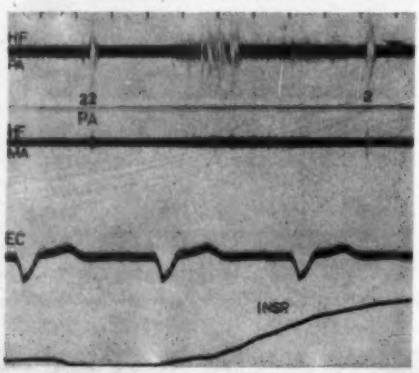

Fig. 10—Left bundle-branch block causing delay in aortic closure and thus reversal of order of valve closure—aortic before pulmonary. On inspiration, pulmonary closure delays as usual and fuses with aortic.

be measured and is a valuable indication of severity (fig. 7). This measurement is difficult to assess clinically since aortic closure may be drowned in the murmur at the pulmonary area and pulmonary closure may be very soft, but it is easily made by taking phonocardiograms simultaneously from the aortic and mitral areas (fig. 6). If there is also a ventricular septal defect, and if the pulmonary stenosis is sufficiently severe to produce a right-to-left shunt (cyanotic Fallot's tetralogy), pulmonary flow is so greatly reduced that pulmonary closure cannot be heard or, even recorded (fig. 8) just as in pulmonary atresia. In a cyanotic patient with pulmonary stenosis, therefore, an audible pulmonary closure sound strongly favours the diagnosis of pure pulmonary stenosis with intact ventricular septum (Leatham 1954), the cyanosis being due to a reversed interatrial shunt. These changes in pulmonary closure are the same whether the stenosis is valvular or infundibular.

By reversed or paradoxical splitting of the second heart sound we mean that the pulmonary valve closes before the aortic; pulmonary closure is delayed as usual

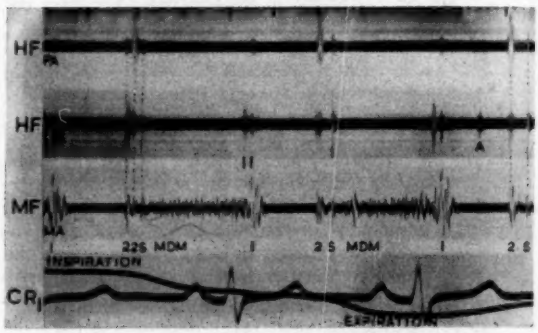

Fig. 11—Mitral stenosis.
Mitral opening snap (s) best shown in recording from lower left sternal edge (L.S.E.). During expiration the snap is too late to be mistaken for pulmonary closure unless this is delayed from complete right bundle-branch block, pulmonary stenosis, or a left-to-right shunt; during inspiration both aortic and pulmonary closure and the snap are shown. There is a gap between the snap and the onset of the ventricular filling murmur. Splitting of the first sound (II) is probably due to delay in mitral closure reversing the order of valve closure.

during inspiration, and thus the splitting of the second sound is narrowed at a time when it would normally be widest (fig. 9). Reversed splitting of the second sound is a valuable physical sign of complete left bundle-branch block (fig. 10); it causes delay in aortic closure, presumably by delaying the spread of conduction since there is no delay in the *onset* of left ventricular systole. Reversed splitting from prolongation of left ventricular systole is found with aortic stenosis, but is more difficult to pick up clinically. It is also found in some patients with patent ductus arteriosus and large left-to-right shunts causing increased stroke volume of the left ventricle, and occasionally with systemic hypertension (Leatham 1952, Gray 1956). In detecting this physical sign it is very important to distinguish between diminution in intensity of all basal heart sounds during inspiration, and diminution in the width of splitting.

Atrioventricular Valve Opening Sounds

Vibrations associated with opening of the atrioventricular valves in early diastole are normally inaudible but become accentuated and audible under certain conditions

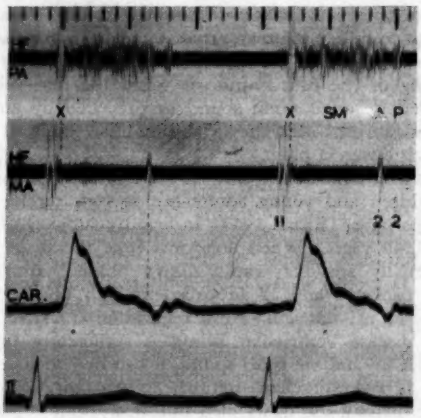

Fig. 13—Mild pulmonary valve stenosis.

Ejection sound (x) at the pulmonary area, occurring very soon after the first sound owing to the short isometric time of the right ventricle. Clinically this extra sound was suspected because the "first sound" in the pulmonary area was loud and snapping in the expiratory phase of respiration and almost disappeared on inspiration. The phonocardiogram shows that both mitral and tricuspid components of the first sound precede the ejection sound. The pulmonary component of the second sound is delayed, causing obvious splitting of the second sound and the pulmonary ejection murmur finishes well before it.

which are not fully understood. Atrioventricular valve stenosis produces very loud opening sounds provided that the valve is mobile, and increased flow from left-to-right shunts may produce soft ones (Leatham and Gray 1956, Neill and Mounsey 1958). The tricuspid and mitral opening snaps are sounds of vastly differing importance. The tricuspid snap occurs in some cases of tricuspid stenosis (Kossman 1955) and in some cases of atrial septal defect; but these sounds are dwarfed by the almost invariably accompanying mitral snap in one instance, and by delayed pulmonary closure in the other, and are thus of little practical value.

The mitral snap (fig. 11), however, is a most important physical sign (Orías and Braun-Menéndez 1939), for, if it is absent, the diagnosis of dominant mitral stenosis is under suspicion. Described by Bouillaud in 1835, its timing and significance were clearly demonstrated by Margolies and Wolferth in a classical paper in 1932. Since then it has been established that it is diminished or abolished by heavy calcification of the mitral valve (Wynn 1953) and is absent in pure mitral regurgitation (Brigden and Leatham 1953). Unfortunately a soft snap may be present when there is too much regurgitation for a successful valvotomy (fig. 28), but in these cases a third sound can usually be heard and recorded in addition.

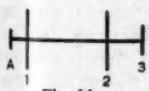

Fig. 14

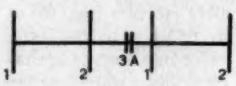

Fig. 15

Fig. 14—Ventricular filling sounds (triple or gallop rhythm).

Atrial sound: hypertension with ventricular hypertrophy; cardiac infarction; aortic or pulmonary valve disease. Third sound: normal (up to 40 years of age); ventricular failure; atrioventricular valve regurgitation; constrictive pericarditis.

Fig. 15—Summation of atrial and third sounds.

Tachycardia. Atrioventricular conduction delay or dissociation. The components of the summation triple rhythm may be normal, or may be abnormally intense, producing a very loud sound.

The old misnomer "reduplication of the second sound" in mitral stenosis emphasises the difficulty in separating the extra sound from splitting of the second heart sound, and it was not until phonocardiograms were taken simultaneously from the pulmonary area and lower left sternal edge (fig. 11), to show both aortic and pulmonary closure and the snap, that we appreciated its true high incidence (Leatham 1952). With this method Mounsey (1953) found a snap in 32 of 33 cases of mitral stenosis. The mitral snap is high-pitched and sharp like aortic or pulmonary closure sounds; it is maximal internal to the apex and at the lower end of the sternum, but is commonly transmitted to the base and is usually obvious at the pulmonary area. It is louder in the expiratory phase of respiration (when splitting of the second sound is minimal), and confusion between it and pulmonary closure can be settled by hearing both aortic and pulmonary closure and the snap during inspiration (fig. 11). It occurs between 0·03 and 0·12 sec. (average 0·07 [Mounsey 1953]) after the onset of aortic closure, according to the relation of the left atrial pressure to the falling left ventricular pressure; but the factors responsible for these pressure relationships are too numerous to allow serious use of this time interval as a measure of the severity of the mitral stenosis (Julian and Davies 1957). That the mitral snap is related to opening of the valve, or to movement of the stenotic valve diaphragm deep into the left ventricle, has not been seriously challenged, but the gap between the snap and the onset of the murmur is rather perplexing (P. Duchosal, personal communication); perhaps the snap is produced at the onset of valve movement before it opens fully.

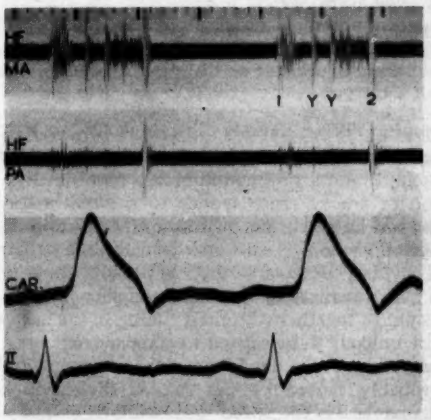

Fig. 16—Extracardiac sounds in a healthy subject occurring around mid or late systole, too late to be related to ejection (0·1 sec. after ejection as calculated from the carotid tracing).

In this subject there was also a systolic murmur which was confined to late systole and was thought to be innocent.

Ejection Sounds

These high-pitched early systolic clicking sounds are related to dilatation of the aorta or pulmonary artery (fig. 12). The pulmonary variety is most commonly associated (though not invariably present) with pulmonary hypertension from any cause, and mild or moderate pulmonary valve stenosis, but not with infundibular stenosis: the aortic variety with coarctation, aneurysm and dilatation, hypertension, stenosis and regurgitation, and the large aorta of Fallot's tetralogy and pulmonary

atresia. Ejection sounds were described as *claquements protosystoliques* by Lian and Welti (1937) and were attributed to opening of the aortic or pulmonary valves (semilunar opening click of Wolferth and Margolies [1945]), but when timed with pressure pulses were found to be due to accentuated ejection vibrations (Leatham and Vogelpoel 1954). An ejection sound resembles late tricuspid valve closure as in complete right branch block (wide splitting of the first sound), but is usually maximal at the base, and the pulmonary variety is much diminished during the inspiratory phase of respiration. The time interval between the onset of the tricuspid component of the first sound and the pulmonary ejection sound varies with the isometric time of the right ventricle, being short with pulmonary stenosis (fig. 13) and long with pulmonary hypertension (fig. 2). The sound is found almost invariably in patients with high pulmonary vascular resistance associated with shunts, but has proved disappointingly uncommon in hypertensive cor pulmonale—perhaps owing to poor transmission of sounds at the base from emphysema, and less enlargement of the pulmonary artery. The aortic variety is less useful because less easy to recognise; there is no respiratory variation and the sound is well transmitted to the mitral and tricuspid areas, making it difficult to distinguish from splitting of the first sound.

Ventricular Filling Sounds (Triple or Gallop Rhythm)

These diastolic sounds comprise the atrial sound, the third sound, and a summation of the two (fig. 14). The addition of one of these sounds to the two main heart sounds, but strangely not of the mitral opening snap or of a systolic sound, is customarily described as triple or gallop rhythm. Because of the low pitch of these sounds, which makes them quite different in quality from all other heart sounds, together with their timing in the heart cycle, they are unlikely to be related to valve movements. They are generally attributed to filling of the ventricles, and they are probably caused by the sudden distension of the ventricular walls; the speed with which this takes place in diastole can be seen when the heart is exposed during a thoracotomy.

Small ventricular filling vibrations can be recorded in normal subjects *following* atrial contraction (Orías and Braun-Menéndez 1939), and larger vibrations in the phase of rapid ventricular filling about 0·15 sec. after the onset of the second heart sound. Accentuation of atrial vibrations so that they become an audible sound is probably always abnormal, while accentuation of rapid filling vibrations produces the third sound which in young subjects is normal.

An atrial sound probably indicates that resistance to ventricular filling is increased. A left atrial sound is most common in systemic hypertension when this is associated with hypertrophy of the left ventricle, and is less common in aortic valve disease (Weitzman 1955). It is not directly related to left ventricular failure. The sound is commonly heard best at the xiphoid, probably because the first component of the first sound is not so loud there. Its pitch is very low, and it needs very gentle application of the bell or else direct auscultation. A right atrial sound may be heard in severe pulmonary hypertension or severe isolated pulmonary stenosis. Atrial vibrations also become audible when they precede the first sound by a greater distance than normal as with partial atrioventricular block (long P-R interval) or atrioventricular dissociation, but these instances can usually be explained by summation (described later). It may be difficult to differentiate an atrial sound from other sounds or short murmurs of similar timing—especially from splitting of the first sound, or when the first sound is followed by an ejection sound or preceded by an atrial systolic murmur—but the atrial sound like the third sound is much lower in pitch.

It is a remarkable fact that the third sound is so common in children and young adults but is very rarely heard, perhaps never (Evans 1943), in healthy subjects over the age of 40 years. When abnormal it is the result of an abnormally speedy "rapid filling phase" from high atrial pressure and is an excellent sign of ventricular failure or of ventriculo-atrial regurgitation. If in mitral valve disease ventricular filling is sufficiently rapid to produce an audible third sound, it can be concluded that there is not sufficient stenosis to warrant valvotomy. Unfortunately the onset of a mitral diastolic murmur is frequently sudden, simulating a third sound, and a phonocardiogram may be required to settle this point. The loudest third sounds are associated with high left atrial pressure from constrictive pericarditis (Mounsey 1955), and when associated with calcification they may be almost as high-pitched as a mitral opening snap. Otherwise third sounds are soft to the ear, which is relatively insensitive to their low pitch, but, if listened for, they are easier to detect than atrial sounds. Because of their low pitch, care is needed not to mistake them for a second sound when the latter is concealed in a pansystolic murmur (figs. 22, 28)—a mistake frequently made in patients with mitral regurgitation. A greater difficulty is in deciding whether a third sound is pure or is followed by a short diastolic murmur.

Summation of the atrial sound on the third sound of the previous cycle is responsible for most of the difficulties in deciding the significance of a triple rhythm; it may be the result of shortening of diastole from tachycardia or from delay in atrioventricular conduction (fig. 15). In either case, normal inaudible atrial and rapid filling vibrations may summate to produce an obvious triple rhythm in the absence of ventricular disease. In healthy children the third sound by itself may be obvious, and summation with atrial vibrations may produce quite a loud triple rhythm.

When both atrial and rapid filling vibrations are abnormally intense, summation from tachycardia produces the most obvious triple rhythm, and the best example is hypertensive heart-failure. Slowing of the heart-rate and separation of the two components is always necessary for a proper analysis of a summation triple rhythm.

Extracardiac Sounds

Extracardiac sounds occur about mid or late systole, after ejection (fig. 16) at a time when the heart is moving in relation to the other mediastinal structures, but no valve movements are taking place. When there is a doubt clinically, a phonocardiogram with a pulse tracing will show that these sounds occur well after ejection. Thus, the timing of these sounds strongly suggests that they are not intracardiac and this is supported by their tendency to great variation with the phase of respiration and with posture. They are entirely innocent, and may be frequently pericardial in origin (Gallavardin 1913), yet they may give a clue to a pneumothorax (Scadding and Wood 1939).

(*The references will appear at the end of the second lecture.*) — pg 757

BLANKETS AND INFECTION
WOOL, TERYLENE, OR COTTON?

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ANTIBIOTIC-RESISTANT strains of pathogenic bacteria have become a serious problem. The *Staphylococcus aureus* in particular is able to acquire resistance faster than new and potent antibiotics can be produced. In the Watford group of hospitals the *Staph. aureus*, phage-type 80, made its appearance towards the end of 1957 and became endemic: all measures taken, including the removal of carriers, cleaning of wounds, repairs to the floors of corridors, wet-mopping, and vacuum cleaning, failed to eradicate it. Despite the most careful control of antibiotic treatment, we encountered 25 cases of infection by erythromycin-resistant staphylococci in the first seven months of 1958. For some time a fresh approach had been essential to eliminate this dangerous organism, and we therefore began to pay special attention to bedding materials.

Blowers, Mason, Wallace, and Walton (1955) showed that blankets and sheets of infected patients harboured the responsible pathogen in large numbers. They found that normal laundering did not sterilise blankets; sterilisation by steam was effective, but blankets so treated shrank and "felted" very badly. Van den Ende, Lush, and Edward (1940) had oiled blankets to prevent dissemination of bacteria. Rountree (1946) and Barnard (1952) had suggested the disinfection of blankets with quaternary ammonium compounds. Blowers and Wallace (1955) confirmed the efficacy of this method, though they were doubtful of its action against *Pseudomonas pyocyanea* and tubercle bacilli.

Blowers, Potter, and Wallace (1957) thought it would be best to make blankets of a material which would not be damaged by boiling. They made trials on three types of material—turkish towelling, 'Loomstate' cotton weave, and synthetic polyester fibre ('Terylene'). They found almost no bacteria after blankets made of any of these materials had been washed at 100°C. These blankets were satisfactory in all respects, except that cotton was more inflammable than wool, and terylene more easily caused static electrical sparking.

Our hospital laundry uses the method of disinfecting woollen blankets with quaternary ammonium compounds described by Blowers and Wallace (1955). In examining test blankets we have found no staphylococci or streptococci, though *Proteus vulgaris* and *Ps. pyocyanea* have survived the process. But the fluff from these blankets seemed to play an important part in the spread of infection, as plates exposed in the wards nearly always revealed numerous colonies of staphylococci around a nidus of fluff. Our experiments were therefore directed towards assessing:

(1) The effect of more frequent cleaning and more careful use of woollen blankets.

(2) The effect of using a blanket material which would not produce fluff.

Method

We devised two experiments to investigate woollen and non-woollen blankets. In both we kept a record of any septic cases in the wards.

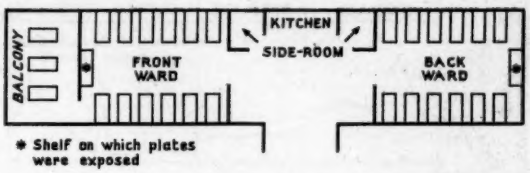

Fig. 1—Plan of the medical unit at Peace Memorial Hospital.

Woollen Blankets

A medical unit at the Peace Memorial Hospital, Watford, was used. This consisted of separate front and back wards, each containing 12 beds. In addition, there were 3 beds at the end of the front ward on a balcony and there was one side-room attached to each ward; but these were discounted for the purposes of the experiment, as they were separate from a bacteriological point of view. Fig. 1 shows the layout of the unit. The front and back wards operated under identical conditions except for bedding.

The front ward was first taken as control, and here the woollen blankets were washed at arbitrary times, depending on the discretion of the ward-sister. The only blankets washed routinely were from infected patients on discharge. In the back ward, all the blankets from each bed were washed as soon as a patient left, and every new patient was given a clean set of blankets. Because we thought that the bacterial content of the bedding might be increased by ambulant patients trailing their blankets on the floor, these patients were not allowed to wrap themselves in blankets from the beds, but were given separate blankets for this purpose. Any patient who was transferred from the front ward to the back ward received a fresh set of blankets.

These conditions operated for eleven weeks. The back ward then reverted to the control status, and for three weeks both wards were under similar conditions. The back ward remained

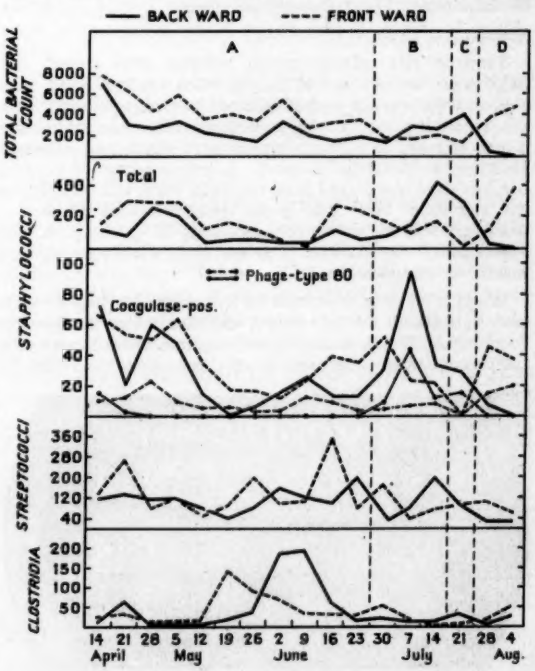

Fig. 2—Bacterial counts at Peace Memorial Hospital.

A—front ward: control
back ward: test
B—both wards: control
C—front ward: test
back ward: control
D—front ward: control
back ward: empty

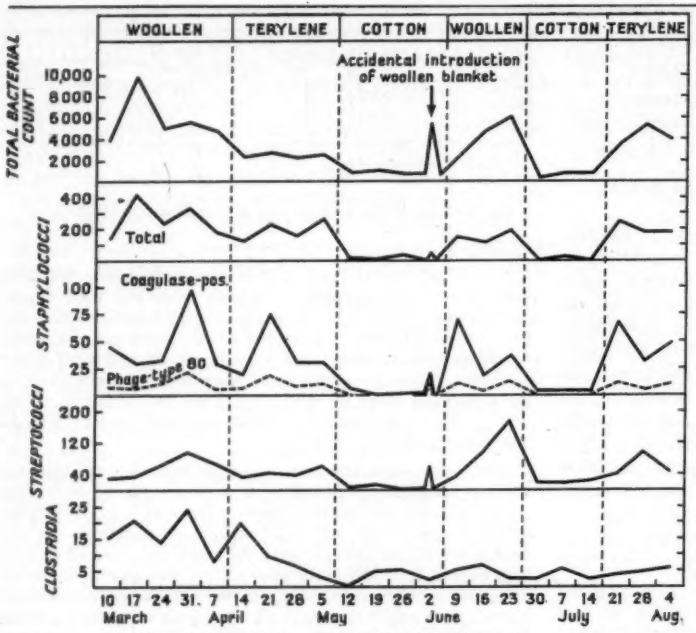

Fig. 3—Bacterial counts at Shrodells Hospital.

as control after that time, and the new system was applied to the front ward. We hoped to continue the experiment like this for three weeks, but unfortunately, after one week the back ward had to be evacuated because its roof began to leak. Some patients were moved to the front ward, and, because of the shortage of clean blankets, the experimental conditions had to be abandoned. Fig. 2 shows these changes.

Non-woollen Blankets

Terylene and cellular cotton blankets were tested, and these were washed at 100°C. Woollen blankets used as a control were washed and disinfected in our usual way. We conducted the experiment in a small side-room containing 3 beds attached to a gynæcological ward which also admitted abortions at Shrodells Hospital. A large number of infected patients were transferred from the main ward, and on entering the side-room each was given freshly washed blankets—woollen, terylene, or cotton—according to the stage of the experiment. No blankets from the main ward were allowed inside the side-room.

Woollen blankets were used for five weeks, terylene blankets were substituted for four weeks, and then cotton blankets for four weeks. Woollen, cotton, and terylene blankets were then used consecutively for periods of three weeks each (fig. 3).

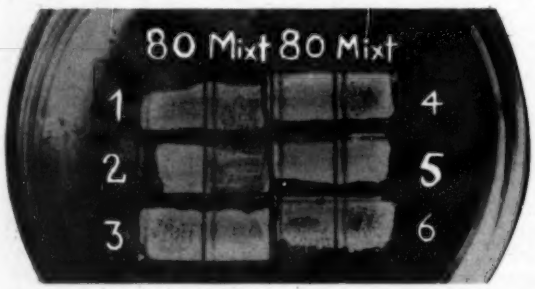

Fig. 4—A typical phage-typing plate. Broth cultures of 6 colonies have been streaked on the plate, and drops of phage 80, and a mixture of groups I and III excluding phage 80, have been added. Only strain 3 exhibits plaques with phage 80 alone, and belongs to phage-type 80.

The purpose of the repetition of the tests was to minimise any error due to climate. The maximum and minimum temperatures for each week were recorded, and also any abnormal conditions, such as gales, which might have influenced the bacterial count. The patients' reactions to new types of blankets were noted.

BACTERIOLOGY

Three types of plate were exposed:

(A) Phenolphthalein phosphate+penicillin.
(B) Blood agar+methyl violet.
(C) Nagler plate+neomycin.

2 plates of each type were used, making a set of 6. They were exposed only on Monday, Tuesday, and Wednesday of each week, leaving the rest of the week for further identification of the organisms isolated. One set of plates was placed in the side-room of the gynæcological ward at Shrodells Hospital, another set was placed on a shelf in the front ward and a third set on an identical shelf in the back ward at the Peace Memorial Hospital (see fig. 1). The plates were exposed between 10.30 A.M. and 2.30 P.M. (which included one round of bed-making), and then incubated overnight—types A and B aerobically, and type C anaerobically—and read the next morning.

Reading of Plates

Type A.—A count of the whole plate gave the total number of penicillin-resistant organisms. The plate was then exposed to a small amount of ammonia vapour, and all red-staining colonies were counted, giving the total number of staphylococci. The red-staining colonies were subcultured on to plain agar, incubated for six to twelve hours, and a slide-coagulase test was made. The coagulase-positive staphylococci were counted; these colonies were subcultured into 0·5 ml. of broth and incubated for six to twelve hours. Strip cultures were then made on plain agar plates, using a wire loop 1 cm. wide. After the plates had dried, one drop of 1/1000 phage 80, and one drop of 1/100 mixture of groups I and III excluding phage 80 (these being the routine test dilutions as previously determined) were placed on each strip and allowed to dry. A known *Staph. aureus*, phage-type 80, was included as control. The plates were incubated at 37°C for five to six hours, left overnight at room temperature, and then read. A count was made of all phage-type 80 staphylococci, these being colonies which were lysed by phage 80, but which exhibited no plaques with the groups I and III mixture (fig. 4).

TABLE I—AVERAGE WEEKLY TOTALS OF COLONIES COUNTED FROM PEACE MEMORIAL HOSPITAL

Organisms	Control ward	Test ward	Test ward count / Control ward count (%)
Total	5014	2757	55
Staphylococci	147	99	67
Coagulase-positive staphylococci	34	27	79
Staph. aureus, phage-type 80	9	1	12
Streptococci	136	138	102
Str. viridans	134	136	102
Str. hæmolyticus, group A	2	1	50
Str. hæmolyticus, other than group A	0	1	..
Clostridium welchii	47	32	68

Type B.—All α-hæmolytic and β-hæmolytic streptococci were counted. Any β-hæmolytic streptococci were subcultured on to blood-agar plates with bacitracin discs, to elicit whether they belonged to Lancefield's group A.

Type C.—All organisms giving a positive Nagler reaction were counted. These were then investigated morphologically and biochemically, and identified.

Results

Bacteriology

The results of the experiment on woollen blankets are shown in fig. 2. The total bacterial count was consistently lower in the ward where clean blankets were provided

TABLE II—AVERAGE WEEKLY TOTALS OF COLONIES COUNTED FROM SHRODELLS HOSPITAL

Organisms	Woollen blankets	'Terylene' blankets	'Terylene' count / Woollen count (%)	Cotton blankets	Cotton count / Woollen count (%)
Total	5545	3654	66	760	13
Staphylococci	241	190	80	12	5
Coagulase-positive staphylococci	49	39	78	2·5	5
Staph. aureus, phage-type 80	9	9	100	1	11
Streptococci	53	50	94	12	23
Str. viridans	50	49	98	12	24
Str. hæmolyticus, group A	1	0	..	0	..
Str. hæmolyticus, other than group A	2	1	50	0	..
Clostridium welchii	18	12	66	4	22

for each new patient than in the control ward. In both wards the counts tended to show weekly fluctuations. When conditions were similar in the two wards, the total count in the back ward was slightly higher than that in the front ward. During the last two weeks of the experiment, bacteria almost disappeared from the empty back ward, whereas the total bacterial count in the front ward rose sharply, because of the cases transferred from the back ward, and the breakdown of routine blanket washing.

The most striking reduction of bacterial numbers in the test ward was of *Staph. aureus*, phage-type 80, which virtually disappeared. During the whole experiment only 4% of coagulase-positive staphylococci in the test ward belonged to phage-type 80, as opposed to 27% in the control ward. The numbers of streptococci and clostridia were little affected. The only clostridium sought and isolated was *Cl. welchii*.

Table I gives the average weekly totals of colony counts, and the percentage of organisms in the test ward as compared with the control ward. The final two weeks of the experiment, and the three weeks during which conditions were the same in both wards, have been omitted. Again there was a marked reduction in the numbers of *Staph. aureus*, phage-type 80. There were a few cases of cross-infection in the test ward, but fewer than in the control ward.

Fig. 3 summarises the second experiment. There was a moderate reduction in total bacterial counts and in the numbers of *Staph. aureus* when terylene blankets were used, but a much greater reduction when cotton blankets were used. With the cotton blankets, there was a great fall in the numbers of coagulase-positive *Staph. aureus* and of *Staph. aureus*, phage-type 80. The numbers of streptococci were little affected by the use of terylene blankets, but they fell when cotton blankets were used, although less than the staphylococci. The count of *Cl. welchii* fluctuated, and bore little relation to the type of blanket used; it was higher after a very windy day, presumably because the spores were airborne.

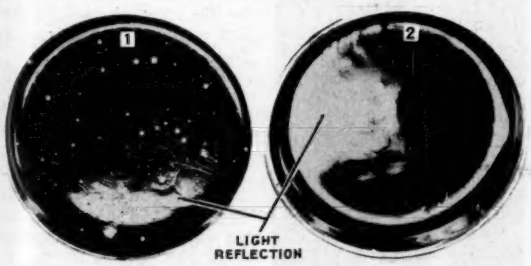

Fig. 5—Methyl violet/blood agar plates. Plate 1 exposed during woollen blanket trial, shows large fragments of woollen fluff and colonisation of bacteria. Plate 2 exposed during cotton blanket trial, shows the fine particles of dust encountered before the blankets' first wash, and fewer bacterial colonies. After washing the particulate matter was not seen. (In order to obtain these pictures, the areas of light reflection were inevitable.)

The fall in bacterial counts when cotton blankets were used could not be attributed to climatic conditions because there was an immediate rise on reintroduction of other blankets. This was confirmed unintentionally on June 3, when a patient with woollen blankets was moved into the experimental side-room, and the blankets were shaken and folded before removal. The total bacterial count that day was 5464. It had been 264 on the previous day, and fell to 252 the next day. The count of *Staph. aureus* showed a similar rise.

Table II gives the average weekly total of colonies counted during this part of the experiment. Cotton blankets produced a much lower count than terylene blankets.

All the time cotton blankets were used there was no cross-infection, even though a patient was admitted to the side-room with multiple lesions produced by *Staph. aureus*, phage-type 80, and this organism was cultured from her nose. During the whole of her stay the count of staphylococci remained low, and repeated nasal swabs of her room-mates produced no growth of *Staph. aureus*.

Throughout the whole experiment, the bacterial counts were not affected by the presence or absence of infective cases nor could they be closely correlated with the climatic conditions.

Differences in the Blankets

The patients found little difference between the terylene and woollen blankets. The terylene ones shrank a little on washing, and after 20 washes they had lost much of their fluffiness and were harder. The nurses noticed that a considerable amount of dust and fluff was emitted from them during bedmaking, and this was reflected in the number of particles on exposed plates.

The nurses also noticed a moderate amount of dust from the new cotton blankets (fig. 5), and they were somewhat critical of the open nature of the mesh. These blankets shrank by about 10% when washed, but this was found to be an advantage because the mesh became closer, and the material was more pliable afterwards. No deterioration was observed after 50 washings But the most important feature was that after washing no dust was noticed and no fluff was found on the plates exposed while cotton blankets were being used. The patients were enthusiastic because they found the cotton blankets as warm as woollen ones but much lighter.

Discussion

The results show that a considerable fall in airborne bacterial counts can be expected if cotton blankets are substituted for woollen ones. A similar though less marked fall followed the use of terylene blankets. Cross-

infection was abolished in the side-room when cotton blankets were used.

Because of the harder-wearing and non-fluff properties of cotton blankets, we believe that they are preferable to terylene blankets. As the first washing removes any dust from the cotton blankets, and also shrinks them to a closer weave, it would be of benefit to wash new blankets before they are used.

We also showed that the use of freshly washed woollen blankets (which should be kept on the bed) for each patient reduced the airborne bacterial counts, and that fewer cases became infected in the ward during this regime. We must emphasise that our results are based on counts of airborne bacteria. Some people believe that these do not give an accurate picture of cross-infection in a ward. But in our experiments, with a limited number of cases, a lowered airborne bacterial count corresponded with a reduced rate of cross-infection.*

The use of cotton blankets with precautions against bacterial contamination would probably result in a great diminution in bacterial counts. We therefore suggest the following measures to combat the spread of infection:

(1) Woollen blankets should be replaced by cotton ones, and these should be washed at 100°C before use.

(2) On admission every patient should be given a bed covered with freshly washed sheets and cotton blankets.

(3) All blankets should remain on the beds. Ambulant patients may have separate blankets, preferably of a distinctive colour, for use when not in bed. These should be washed regularly, as they are very likely to pick up bacteria from the floor.

Summary

We made two experiments to assess the effect of blankets on bacterial infection in hospital.

The first experiment showed that the use of freshly washed blankets, disinfected with quaternary ammonium compounds, for each patient admitted to a test ward, reduced the total bacterial count (and especially the *Staphylococcus aureus*, phage-type 80, which was previously endemic) and also decreased cross-infection.

The second experiment showed that there was a moderate reduction of the total bacterial count when terylene blankets were used instead of woollen blankets. But the total bacterial count was reduced more, and there was no cross-infection, during the time that cotton blankets were used. After the first washing cotton blankets did not produce the fluff which seems to be a major factor in the spread of infection.

Our thanks are due to Dr. A. R. Kelsall and Mr. D. J. MacRae who helped to plan the experiments, and to Dr. R. E. O. Williams of the Public Health Laboratory, Colindale, for tuition in phage-typing procedures. We would also like to thank the matrons and nurses of the Peace Memorial Hospital and Shrodells Hospital for their cooperation.

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* Experiments are being performed to establish whether the protein in woollen blankets allows staphylococci to remain viable for longer than on cotton blankets. Small squares of new blanket material, both woollen and cotton, are inoculated with 120 viable *Staph. aureus*, phage-type 80. For the first two weeks these are impressed on agar and immersed in both at two-day intervals. Later cultures are made every week. In preliminary tests we have failed to culture staphylococci from the cotton squares seven days after inoculation, while the woollen squares still harbour the viable organisms at thirty days.

THE FIBRE COMPOSITION OF HOSPITAL DUST

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INFECTION of wounds in hospitals, particularly with penicillin-resistant strains of *Staphylococcus aureus*, has become a world-wide problem. There is general belief that the hospital blanket is a source of infection and that the infective bacteria are readily disseminated whenever the blanket is disturbed, as in bedmaking.[4] A big increase in the bacterial count of air samples when beds are being made in the vicinity of the sampling position has been demonstrated,[13] and the oiling of bedclothes—particularly blankets—to reduce the amount of dust has frequently been suggested.[8 10 12 15–18] However, there is no definite evidence that sterilisation of hospital blankets will prevent or reduce wound infection,[2] and in several ward trials regular blanket sterilisation has had no significant effect on the incidence of infection.[1 12] The presence of *Staph. aureus* in an extremely wide range of places in the hospital,[6 11] the scattering of infected material from skin and from clothing in spite of normal gowning,[5 7] and the possibility of infection taking place in the operating-theatre [2 3 9 14] have to be considered.

As part of an investigation of the hospital blanket problem it was thought desirable to make a direct examination of hospital dust—presumably the vehicle chiefly responsible for carrying bacterial infection to a wound. For this purpose samples were collected in three hospitals in the Melbourne area.

Method of Dust Collection

A preliminary sample of floor sweepings contained a high proportion of heavy debris that would never be airborne, and sampling from the air at bed height was therefore undertaken.

The dust collector (see figure) consisted of a ' Ventaxia ' fan (diameter 6 in.) mounted on a wooden frame so that its centre was 34 in. above the floor. A circle of fine ' Terylene ' curtain fabric (approximately 100 warp and weft threads per inch, and with a pore size of about 0.1 mm. diameter) was fastened by means of a spring band to the inlet side of the fan. The efficiency of the filter was increased by the electrostatic charge acquired by the terylene and by the mat of fibres forming on the surface of the fabric.

The dust collector.

After the collector had run for 24 hours in a ward, about 48 mg. of dust, essentially fibrous in nature, had collected on the filter. Bacteriological examination of samples from all three hospitals showed coagulase-positive *Staph. aureus* (in twelve of fourteen samples tested). The results of detailed bacteriological examination of the dust will be reported

COMPOSITION OF AIRBORNE FIBRES

Hospital	Sample no.	Fibres counted	Numerical percentage composition		
			Cellulose	Protein	Unidentified or others
A	1	310	94·5	1·3	4·2
	2	319	97·5	2·5	0
B	1	181	98·9	1·1	0
	2	285	95·6	4·4	0
	3	—	100·0	0	0
	4	97	94·8	5·2	0
	5	219	94·5	5·5	0
	6	205	91·2	5·8	3·0
	7	169	95·8	3·5	0·7
	8	173	96·5	3·5	0
	9	184	92·9	7·1	0
	10	144	95·1	4·9	0
	11	169	100·0	0	0
	12	184	97·3	2·7	0
	13	183	100·0	0	0
C	1	268	94·8	5·2	0
	2	255	94·3	5·3	0
	3	175	97·5	1·1	1·4
	4	275	98·0	1·5	0·5
	5	198	97·2	0	2·8
	6	177	95·2	4·8	0
	7	272	95·3	4·3	0·4
Average of 22 samples			96·2	3·2	0·6

Samples B10, 11, 12, and 13 were taken in a theatre during operations, B3 from the theatre air exit, and C6 from an internal corridor serving a group of four theatres. "Other fibres" included nylon, acetate, mould hyphæ, and a few unidentified fibres.

separately by A. Gardner and K. G. Pope. For comparative purposes dust was collected from the floor directly below the machine and from the hospital floors in general, using a broom or vacuum cleaner.

Fibre Composition of Dust

In all samples other than floor sweepings, fibres were the chief constituent. Often during sweeping the broom collected grit, but fibres formed rolls which passed under the broom and remained on the floor. Where a vacuum cleaner was used the material collected was fibrous. Airborne dust, which is of greater importance in cross-infection, contained little non-fibrous material.

Identification of fibres was aided by heating a portion of the dust in a three-dye mixture.* This reagent stained cellulose pink, cellulose acetate yellow, protein blue, and nylon green, while 'Orlon' and terylene remained almost unstained. The dyed fibres were recovered by vacuum filtration through a sintered glass gooch crucible, washed on the filter, and mounted on a microscope slide with glycerol-water. Any fibres not immediately recognised at ×70 were examined at ×420 and compared with illustrations in standard fibre atlases or with known fibres. To determine the relative proportions of the different types of fibre, the slides were examined at ×70 using an eyepiece with cross wires. Counts were made of fibres touching the cross wires in six randomly selected fields on each slide, and the results recorded as the percentage of the total number of contacts with cellulose, protein, and other fibres.

All samples were found to be predominantly cellulose. Even the rolls of fluff left by the broom and considered on macroscopic examination to be wool, averaged (on a numerical basis) 60% cellulose and 40% protein. The airborne dust was nearly pure cellulose, as shown in the table. Not all the protein fibres were wool: feather fragments were found in all hospitals and fur fibres in two. The presence of these unexpected fibres, together with nylon and cellulose acetate, indicates that some of the wool fibres collected may well have originated in apparel. The cellulose fibres would presumably come from sheets, towels, clothes worn by hospital staff and visitors, wound dressings, and bandages. Since dust from hospital B (see table), which uses all-wool blankets, shows a fibre distribution similar to that from hospitals A and C, in which wool-cotton union blankets are used, it is unlikely that the cotton warp of the union blankets contributed materially to the airborne cellulose.

* The dye solution consisted of: 'Solar Scarlet RL' (Sandoz), 3 g.; 'Artisil Direct Yellow RGFL' ultra-dispersed (Sandoz), 3 g.; 'Brilliant Alizarine Milling Blue RWL' (Sandoz), 5 g.; sodium sulphate, hydrated, 10 g.; sulphuric acid, concentrated, 10 ml.; water to make 1 litre.

A small composite sample of fluff was collected with forceps from various sites on the filter and placed in a 75×10 mm. test-tube; 0·8 ml. of dye was then added, and the tube heated for five minutes in a boiling-water bath.

Summary and Conclusions

All samples of airborne dust collected in three hospitals consisted essentially of cellulose fibres. Very few wool fibres could be found. Most samples subjected to bacteriological examination contained coagulase-positive *Staphylococcus aureus*. This suggests the cross-infection with *Staph. aureus* is primarily due to transfer of the bacteria by some agency other than fluff from blankets, and that therefore replacement of wool blankets with those made from other textile fibres, or the application of an oiling technique to blankets only, is unlikely to reduce cross-infection.

The collection of dust samples was arranged by Mr. C. G. Rankin (manager) and Mr. G. Buckle (bacteriologist) at the Alfred Hospital, by Dr. R. B. Maynard (senior pathologist) and Mr. K. G. Pope (senior bacteriologist) at the Repatriation General Hospital, and by Dr. D. Cowling (clinical pathologist) at the Royal Melbourne Hospital. Bacteriological examinations were made by the laboratories of the hospitals concerned and by Mr. W. G. Crewther, senior principal research officer, at the C.S.I.R.O. laboratories.

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SALMONELLA TYPHIMURIUM INFECTION DUST-BORNE IN A CHILDREN'S WARD

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THE importance of floor sweepings and dust as the means of cross-infection by intestinal organisms in hospital wards has been firmly established for enteropathic strains of *Escherichia coli* by Rogers (1951). Little attention has been paid to the transmission of salmonella infections in this way; Rubbo (1948) isolated *S. derby* from samples of dust during an outbreak of infection in an infants' ward, and Neter (1950) found strong evidence that *S. oranienburg* was transferred, by dust, from the throat of an infected infant to the alimentary tract of two other children.

CHRONOLOGY OF THE EPIDEMIC

Infants	Case no.	Date of admission	First symptoms of infection	Duration of symptoms	Duration of infectivity
Episode 1:					
15 at risk	1	Dec. 21, 1956	Dec. 26, 1956	30 days	5 weeks
5* infected	2	„ 24, „	„ 31, „	8 days	3 weeks
	3	Nov. 23, „	Jan. 2, 1957	30 days	6 mos.
	4	Jan. 10, 1957	„ 16, „	14 days	2 weeks
	5	June 26, 1956	„ 18, „	30 days	7 mos.
	6	Nov. 13, „	Symptomless excreter		3 mos.
Episode 2:					
14 at risk	7	Jan. 30, 1957	Feb. 2, 1957	15 days	4 mos.
2 infected	8	„ 31, „	„ 7, „	13 days	?
Episode 3:					
14 at risk	9	March 15, 1957	March 22, 1957	14 days	2 weeks
3 infected	10	„ 16, „	April 8, „	7 days	3 weeks
	11	April 10, „	„ 16, „	7 days	17 weeks
Episode 4:					
3 at risk	12	May 4, 1957	May 9, 1957	2 days	?
1 infected					
Episode 5:					
5 at risk	13	June 18, 1957	June 26, 1957	2 days	?
1 infected					
Episode 6:					
18 at risk	14	Aug. 9, 1957	Aug. 17, 1957	24 hours	?
6 infected	15	„ 9, „	Sept. 5, „	†	?†
	16	„ 13, „	Aug. 18, „	9 days	4 weeks
	17	Sept. 4, „	Sept. 10, „	3 days	?
	18	„ 5, „	„ 17, „	2 days	?
	19	„ 12, „	„ 17, „	2 days	?
Episode 7:					
10 at risk	20	Oct. 24, 1957	Oct. 31, 1957	†	?†
2 infected	21	„ 25, „	Nov. 17, „	2 days	?

* Case 6, believed to have been infected before admission, is not included.
† Transferred to another hospital.
? indicates that the patient was still excreting *S. typhimurium* on discharge.

In the outbreak we describe, dust-borne organisms appear to have kept alive a *S. typhimurium* infection which brought a cubicle ward in a children's hospital virtually to a standstill for 11 months in 1956 and 1957. Twenty-one infants were affected but none were seriously ill. This is not always so; there are reports of many hospital outbreaks with a considerable mortality. In a recent review of salmonella meningitis, Watson (1958) reported a case-mortality of 100% from *S. typhimurium* in infants. Mackerras and Pask (1949) suggested that carriers of this organism in infancy are as dangerous as carriers of *S. typhi*. Because our patients were vulnerable, by reason of age and pre-existing illness, and because there was always the possibility of a sudden increase of virulence, we had to evacuate and clear the ward whenever a patient became infected.

The affected ward, which is used for the isolation of all infants under one year of age who are not suffering from gastroenteritis, is a self-contained unit apart from the supply of feeds which come from a central milk-kitchen. There are six single and three double cubicles surrounding an open ward with four cots. Each cubicle is equipped with bath and washbasin, and paper hand towels are used. Gowns are provided for the doctors and nurses attending the baby. During the epidemic, the open part of the ward was not used for infants, and each double cubicle had only one occupied cot, thus assuring complete isolation for each patient. The usual practice of culturing the stools of each baby on admission was continued, and it was planned to re-examine the stools twice weekly.

History of the Epidemic

First episode.—A child admitted on Dec. 21, 1956, with bronchitis, passed green mucoid stools 5 days later. The second patient, admitted with an upper respiratory infection on Dec. 24, developed diarrhœa within 7 days, while the third patient, who had been treated for cerebral palsy for 5 weeks, developed diarrhœa on Jan. 2, 1957. *S. typhimurium*, phage-type 2, was isolated in each case. All three were transferred elsewhere for isolation, and the ward was closed to further admissions pending bacteriological investigation of the staff and remaining patients. Two of these patients developed diarrhœa, and one symptomless intermittent excreter was found. This child had been admitted on Nov. 13, 1956, because he failed to thrive after treatment of a non-specific gastroenteritis in another hospital. No salmonella had been isolated from a stool swab on admission, and when his stools were investigated during the outbreak *S. typhimurium* was found in only 2 out of 9 specimens; but he may have been responsible for introducing the infection.

When the last patient was removed, the walls, floor, furniture, and plumbing fixtures were surveyed bacteriologically. *S. typhimurium*, phage-type 2, was isolated from the meshes of the wicker basket of the weighing-machine (cf. Rogers 1951) but from nowhere else. No excreters were found among the nursing or domestic staff. The ward was washed down, the cubicles were fumigated with formalin spray, and the wicker basket was replaced by one made of plastic material.

Second episode.—On the day that the ward was reopened (Jan. 30, 1957) a child was admitted with bronchitis. No pathogens were isolated on admission from a routine stool specimen but after 3 days he developed diarrhœa. A second infant, admitted on Jan. 31, developed diarrhœa 7 days later. *S. typhimurium*, phage-type 2, was isolated from both patients. The ward was closed, washed down, and sprayed with formalin; investigation of the staff was repeated and this disclosed that a nurse had become a symptomless excreter.

Third episode.—The ward opened again on Feb. 20. A child of 2 months was admitted on March 15 because of feeding mismanagement. There were no pathogens in the routine stool swab on admission, and the ward had been free from infection for 3 weeks, but 7 days later diarrhœa developed. A child admitted on March 16 developed diarrhœa on April 8, and another child admitted on April 10 developed diarrhœa 6 days later. From all three *S. typhimurium*, phage-type 2, was isolated.

This time, besides closing and clearing the ward, we decided to examine bacteriologically the whole medical, nursing, and domestic staff, and the porters of the hospital. The orderly in the ward under investigation, the orderly in a ward for older children, and two porters were found to be excreters.

Fourth episode.—The ward reopened on May 4. A child admitted that day because of feeding mismanagement developed diarrhœa 5 days later. The ward was again closed, and after the usual routine of cleaning and bacteriological investigation of the staff, it was opened for older children at the beginning of June. When there had been no case of *S. typhimurium* infection for 2 weeks, infants were again admitted.

Fifth episode.—A child admitted on June 18 developed diarrhœa 8 days later and *S. typhimurium* was again isolated. After emptying the ward and investigating along the lines previously followed it was opened again on July 18.

Sixth episode.—The next case of diarrhœa in which *S. typhimurium* was found was on Aug. 17. Five further infants developed diarrhœa during the next 5 weeks, though one of these was at home after discharge.

For the sixth time in 8 months the ward was closed and disinfected, and the staff were subjected to the most drastic investigation. Three nurses who had been involved in all the outbreaks were examined serologically and were given purgatives in an attempt to find a carrier, but without success.

Seventh episode.—The ward was opened for older children on Oct. 16, and, when there had been no infection for a week, babies were again admitted. An infant was accepted from a maternity hospital on Oct. 24, because of multiple congenital defects, and 7 days later developed diarrhœa. A child, admitted on Oct. 25 and discharged on Nov. 7, developed diarrhœa 10 days after discharge. *S. typhimurium* was isolated from both cases.

The Source of the Infection

Clearly the infection was being disseminated neither by a human carrier nor by food. All the babies were milk-fed, and all feeds were prepared in a central milk-kitchen which operates under constant bacteriological control and which supplies feeds to other wards unaffected by this infection. We concluded that the infection must be in the physical environment of the ward and that our previous efforts at disinfection by washing and spraying had been ineffective. We therefore decided to subject the ward and its contents to the most rigorous and thorough disinfection. Every suitable object was sterilised by steam, the entire unit (wards, kitchen, sluice, and all store-cupboards) was fumigated with gaseous formaldehyde (*Extra Pharmacopœia* 1941), and all destructible ward stores were burned—including brooms, floor-cloths, dish-cloths, and dusters.

While this disinfecting process was in preparation the cleaning arrangements of the ward were scrutinised. The floors had been swept with a soft broom, and during the epidemic samples of floor dust had failed to reveal *S. typhimurium*. A Columbus Dixon, model no. 3, floor-polisher of the type which incorporates a vacuum dust-bag had also been used. Since this was not regarded as a vacuum-cleaner, the bag had been emptied only infrequently. When its contents were examined in November, 1957, a high concentration of *S. typhimurium*, phage-type 2, was found. This organism still remains viable in the bag 10 months after the removal of the last case from the ward.

We therefore decided, when the ward was opened after fumigation, to abandon sweeping in favour of suction-cleaning (using a cylinder-type vacuum-cleaner with disposable paper bags) and to modify the floor-polisher so that the dust-bag was lined by a destructible paper container. Since this change was made at the end of November, 1957, the ward has been in full use without further infection.

Discussion

The *S. typhimurium* infection was probably introduced in November, 1956, by the child who had non-specific gastroenteritis in another hospital and whom we found to be an intermittent excreter. Even at this early stage there was evidence of an environmental infection in the finding of these organisms in the weighing-machine basket.

On investigation of the second and third outbreaks a nurse, two orderlies, and two porters were found to be excreters. It seemed highly probable that the porters had been infected by handling contaminated linen, but they were unlikely to have conveyed infection to patients, because their sole duty in the ward was the collection of soiled linen.

In the last four outbreaks no human carrier was detected, and, as we have explained, it was not possible that the infection had come from the milk-kitchen. We therefore had reason to believe that the infection was environmental. This was confirmed by the finding of *S. typhimurium*, phage-type 2, in the bag of the floor-polisher. It seemed likely that dust contamination by passage of organisms through the porous bag of this machine was the cause of the later outbreaks, and may have been responsible for all but the first.

Summary

In the infants' ward of a children's hospital seven outbreaks of gastroenteritis over a period of 11 months were caused by *Salmonella typhimurium*, phage-type 2.

The infection was not being spread by human carriers nor from the central milk-kitchen. Finally the source was found in the dust-bag of a vacuum floor-polisher.

Since suction-cleaning and polishing of the floors by machines fitted with disposable paper dust-bags has been substituted, there has been no case of *S. typhimurium* infection.

We are much indebted to Dr. Joan Taylor and Dr. E. S. Anderson for confirmation and phage-typing of the organisms isolated, to Dr. Joan Taylor and Dr. R. E. O. Williams for their help and advice during the epidemic, and to Messrs. Columbus Dixon for quickly producing an effective modification of their polishing machine.

The burden of the epidemic and of its final elimination fell heavily on the nursing staff, for whose willing help and cooperation we are most grateful.

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ANTIDIURETIC ACTIVITY IN THE BLOOD AFTER STIMULATION OF THE NEUROHYPOPHYSIS IN MAN

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WATER diuresis can be inhibited in man by the intravenous injection of 1–10 milli-units of vasopressin (Theobald 1934, Barclay and Cooke 1950, Burn and Singh Grewal 1951, Lewis 1952). As this represents a maximum concentration in the blood of 0·002 milli-units per ml., it is unlikely that the concentration of antidiuretic hormone (A.D.H.) in the blood under normal conditions is sufficiently high to be detected by present methods of bioassay.

Antidiuretic activity equivalent to 0·24–5·5 milli-units A.D.H. per ml. has been reported in human serum or plasma (Lloyd and Lobotsky 1950, Slessor 1951, Hawker 1952, Stein et al. 1954), but the method of assay was to inject serum or plasma either intraperitoneally or subcutaneously into hydrated rats. The use of serum is illogical, as it inactivates A.D.H. (Dicker and Ginsburg 1950, Ames and van Dyke 1952, Heller 1952). Moreover, assays of antidiuretic activity in body fluids vary widely according to the route of injection into the test animal (Noble et al. 1939, Dicker 1953, Ginsburg and Heller 1953b, Erspamer and Sala 1954), and, unless the intravenous route is used, values may be grossly enhanced (Ames and van Dyke 1952, Lewis 1952, van Dyke et al. 1955).

In our own work a method of extraction and intravenous assay is used to estimate antidiuretic activity in human blood (Bisset and Lee 1957a). In a recent series of 13 patients activity could not be detected in a single instance in " peripheral " blood (blood from the extremities) (Lee and Bisset 1958), although the assays were capable of detecting from 0·001 to 0·015 milli-units A.D.H. per ml. of blood. Other workers using intravenous assay techniques have reported mean levels of antidiuretic activity in " peripheral " blood of normal subjects equivalent to $<0·0125$ or $<0·020$ milli-units A.D.H. per ml. (Robinson et al. 1957, Macfarlane and Robinson 1957).

The purpose of the present investigation was to determine whether antidiuretic activity could be detected in "peripheral" blood after stimulating the neurohypophysis. The stimulus consisted of smoking cigarettes, or inhaling amyl nitrite, during water diuresis. Antidiuretic activity was assayed in both blood and urine. The probable amount of A.D.H. released from the neurohypophysis during stimulation was deduced from the amount of antidiuretic substance excreted in the urine. The theoretical level of A.D.H. in the blood was calculated, and this was compared with the observed level of antidiuretic activity. The investigation was confined to the antidiuretic hormone of the neurohypophysis, as there is no observable effect of the release of oxytocin during water diuresis, nor is there a reliable method for estimating this hormone in urine.

Methods

The subjects were non-smokers in a sitting position.

Water diuresis was induced by drinking 1200–1600 ml. of water. When the diuresis had reached a satisfactory level, the subjects smoked 3–6 cigarettes in succession or inhaled amyl nitrite. From each subject one sample of blood was collected during the initial diuresis, followed by a second and, in 1 case, by a third sample during the period of inhibition of diuresis. The blood was withdrawn from the median cubital vein into siliconed syringes. Urine was passed voluntarily at intervals of fifteen minutes; each specimen was acidified with normal sulphuric acid.

Assay of Antidiuretic Activity in Blood and Urine

Extracts were prepared from blood by the method of Bisset and Lee (1957a). In some experiments urine was neutralised with normal sodium carbonate and tested for antidiuretic activity without further treatment; in other experiments extracts were prepared from urine by the method of Noble et al. (1939). All extracts and urine were assayed against A.D.H. ('Pitressin,' Parke Davis) by intravenous injection into the anæsthetised rat (Ames and van Dyke 1952). Control experiments were carried out in which a known amount of oxytocin or A.D.H. was added to blood or urine, and an extract prepared for the assay of exogenous activity. The recoveries of activity from blood were 60%, 60%, 93%, 45%, 106%, 63%, and 46%. In those experiments in which extracts were prepared from urine the recoveries were 44%, 38%, and 39%. The figures given in the results for endogenous antidiuretic activity in blood and urine have been corrected according to the recoveries obtained in each case, and are expressed in terms of A.D.H.

Specimens of extracts or of urine containing antidiuretic activity were treated with 0·01 *M* sodium thioglycollate, which abolishes the activity of neurohypophysial hormones (van Dyke et al. 1942).

Results

From evidence presented here and in previous work, we believe that the antidiuretic activity detected in blood and urine is due to the antidiuretic hormone of the neurohypophysis. But, in order to avoid any unwarrantable assumption, results will be expressed in terms of milli-units of "antidiuretic substance" (A.D.S.).

Effect of Smoking

In the first series of experiments, which were carried out on three subjects (1–3), extracts were prepared from pooled specimens of urine.

The results obtained with subject 1 are illustrated in fig. 1. The experiments were carried out in an analogous fashion on the other two subjects.

Subject 1 smoked 5 cigarettes in 46 minutes and experienced nausea, pallor, and sweating for 30 minutes. During the period of antidiuresis (B), which lasted for 195 minutes, 85 milli-units of A.D.S. were excreted in the urine. None was detected during either of the periods of diuresis (A and C). The level of A.D.S. in the blood during smoking (Y) was 0·007 milli-units per ml. Activity was not detected in the blood before smoking (X) (<0·008 milli-units per ml.).

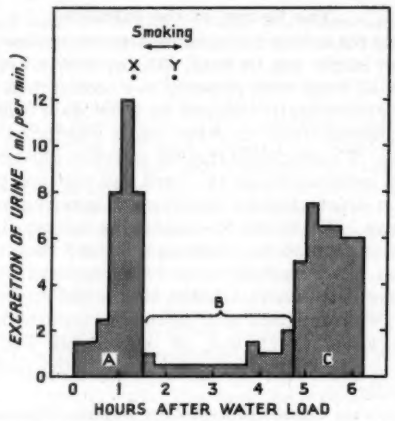

Fig. 1—Effect of smoking on water diuresis in subject 1.
During period of smoking subject smoked 5 cigarettes. Blood withdrawn from median cubital vein contained <0·008 milli-units A.D.S. per ml. at X and 0·007 milli-units A.D.S. per ml. at Y. Specimens of urine were pooled during periods A, B, and C, which represent respectively initial diuresis, antidiuresis, and subsequent recovery. Total amounts of A.D.S. excreted in urine were: A, <0·4 milli-units; B, 85·3 milli-units; C, <0·6 milli-units.

Subject 2 smoked 3 cigarettes in 33 minutes and experienced nausea and giddiness. Diuresis was inhibited for 150 minutes. The amount of A.D.S. excreted in the urine during the initial diuresis (A) was 1·2 milli-units and during the antidiuresis (B) 57 milli-units. Activity was not detected during the period of recovery (C). The level of A.D.S. in blood collected 8 minutes after smoking had ceased was 0·040 milli-units per ml., but, before smoking, activity was not detected (<0·008 milli-units per ml.).

Subject 3 smoked 6 cigarettes over a period of 45 minutes. Sweating, dizziness, and nausea were experienced. Diuresis was inhibited for more than 12 hours, and the inhibition of diuresis was accompanied by a persistent headache which resembled migraine. During the initial period of diuresis (A) 3·4 milli-units of A.D.S. were excreted in the urine; antidiuretic activity was not detected in the blood before smoking (<0·005 milli-units per ml.). During the period (B), which was arbitrarily terminated 195 minutes after the commencement of antidiuresis, 259 milli-units of A.D.S. were excreted. The level of A.D.S. in blood collected 5 minutes after smoking had ceased was 0·017 milli-units per ml. In blood collected 100 minutes later, when diuresis was still inhibited, antidiuretic activity was not detected (<0·017 milli-units per ml.).

This series of experiments indicated total amounts of A.D.S. excreted in the urine. In a second series, which was carried out on four subjects (1, 3, 4, and 5), urine was collected at intervals of 15 minutes and each specimen was assayed, without extraction, for antidiuretic activity. The rates of excretion of urine and of A.D.S. for subject 1 are shown in fig. 2.

The response of subject 1 was similar to that observed in the previous experiment (cf. fig. 1). Diuresis was inhibited for 165 minutes. The total amount of A.D.S. excreted in the urine was 74 milli-units. During the first period of 15 minutes after the antidiuresis started—i.e., from 1¾ to 2 hours after the water load—the rate of excretion of A.D.S. was 1·0 milli-units per minute and diuresis was almost completely inhibited. In the second period A.D.S. was excreted at a rate of 1·75 milli-units per minute; this was the highest rate recorded. During the third, fourth, and fifth periods the rates of excretion were 1·4, 0·1, and 0·65 milli-units per minute respectively.

Although antidiuresis persisted during the next six periods, antidiuretic activity was no longer detectable in the urine. In fact, at one point the rate of excretion of A.D.S. was <0·03 milli-units per minute.

In subjects 3 and 5 vigorous smoking, which was accompanied by nausea and dizziness, had no effect on water diuresis and activity was not detected in any of the samples of urine. In subject 4, smoking caused moderate inhibition of diuresis, but the rate of excretion of A.D.S. was <0·1 milli-units per minute. In subjects 3–5 samples of blood collected before and after smoking did not contain detectable antidiuretic activity (i.e., <0·009 milli-units per ml. of blood in all subjects).

Effect of Amyl Nitrite

An experiment to test the effect of amyl nitrite is illustrated in fig. 3.

The subject (3) sat throughout the experiment. When the nitrite was inhaled, the blood-pressure fell from 120/80 to 100/60 mm. Hg. Blood was collected when the subject was on the point of syncope. Diuresis was inhibited briefly, but antidiuretic activity was not detected in either blood or urine.

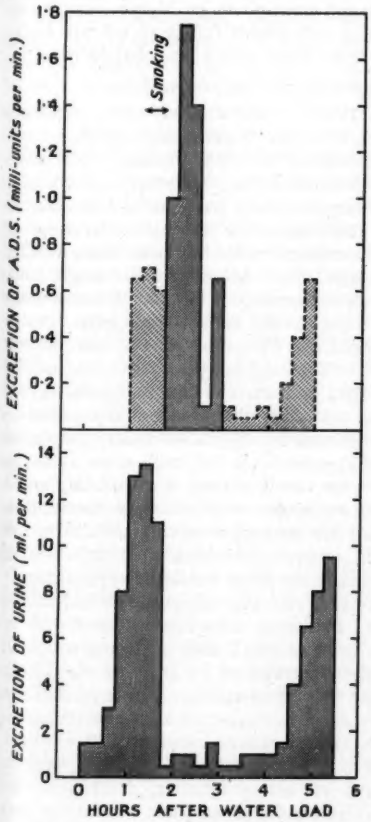

Fig. 2—Effect of smoking on water diuresis in subject 1.

During period of smoking subject smoked 4–5 cigarettes. Blood was not taken for A.D.S. estimation. Urine was collected at intervals of 15 minutes, and each specimen was assayed for antidiuretic activity. Above: dark shaded area shows rate of excretion of A.D.S. in urine; light shaded area indicates that activity was not detected in urine and signifies limit of sensitivity of assay, which varies with rate of excretion of urine.

Discussion

Effect of Smoking on the Neurohypophysis

The antidiuretic action of nicotine was first demonstrated in the rat and in man by Burn et al. (1945).

Taylor and Walker (1951) detected an antidiuretic substance in the urine after smoking which had activity equal approximately to 50 milli-units pituitary (posterior lobe) extract. In an extension of this work, Burn and Singh Grewal (1951) demonstrated the excretion of 95 milli-units in the pooled urines of two individuals in whom smoking had caused inhibition of diuresis lasting for 195 and 105 minutes. In another individual, in whom the inhibition lasted for 180 minutes, 75 milli-units were excreted. But in three other cases, in which the inhibition lasted for 60, 105, and 105 minutes, no antidiuretic activity was detected. Both groups of workers prepared extracts from urine by the method of Noble et al. (1939) and tested these extracts by subcutaneous injection into hydrated rats (Burn 1937).

In the first series of experiments reported in this paper extracts were prepared from urine by the same method, but the assays were carried out by intravenous injection in rats. Noble (1957) has stated that concentrated extracts of urine contain pressor activity which might interfere with any method of assay by intravenous injection. We tested an extract, concentrated 100 times, on the blood-pressure of a rat and observed only a depressor effect.

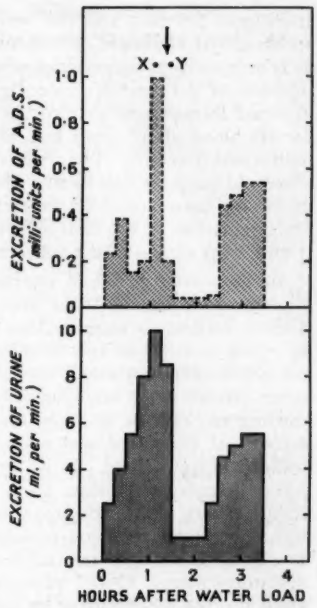

Fig. 3—Effect of amyl nitrite on water diuresis in subject 3.

At point indicated by arrow subject inhaled amyl nitrite. Blood withdrawn from median cubital vein contained <0·015 units A.D.S. per ml. at X and <0·017 units A.D.S. per ml. at Y. A.D.S. was not detected in urine, and light shaded area has same connotation as in fig. 2.

The antidiuretic effect of extracts from urine passed after smoking could not have been due to nicotine excreted in the urine, as this substance inhibits diuresis in the rat under ethanol anæsthesia only in doses which cause respiratory arrest. Finally, the fact that activity was abolished by sodium thioglycollate suggests that the antidiuretic substance (A.D.S.) in extracts from urine is identical with A.D.H.

In this first series of experiments, one of which is illustrated in fig. 1, the amounts of A.D.S. excreted in the urine after smoking were 85, 57, and 259 milli-units. That this activity was causally related to the inhibition of diuresis is shown by the fact that, in subjects 1 and 2 the urine collected during the recovery periods contained no antidiuretic activity. In subject 3, in whom 259 milli-units were excreted, there was no recovery of diuresis during the period of the experiment. If vasopressin is injected intravenously in man, approximately 8·5% of the antidiuretic activity may be recovered from the urine; this figure has been calculated from data by Burn and Singh Grewal (1951) and Noble and Taylor (1953). Hence, if A.D.S. is identical with A.D.H., subject 1 secreted about 1 unit, subject 2 about 0·7 unit, and subject 3 about 3 units. The neurohypophysis of the adult contains about 15 units A.D.H. (Heller and Zaimis 1949). It is a striking fact that in subject 3 smoking caused the release of a fifth of such an amount from the neurohypophysis, and yet the level of A.D.S. in the blood was only 0·017 milli-units per ml.

In all three subjects A.D.S. was present in the blood after, but not before, smoking. The highest level was 0·040

milli-units per ml.; and this was observed in subject 2, in whom the inhibition of diuresis was the most brief. If it is supposed, as an extreme case, that the whole of the amount of 0·7 unit secreted by this subject had been released instantaneously into the blood-stream, the level in the blood alone could not have exceeded about 0·14 milli-units per ml. The relatively high level actually observed suggests that in this case the time at which the blood was taken coincided with a high level of hormone in the circulation. It has then to be supposed that in subjects 1 and 3 the timing of the collections was less propitious.

In the second series of experiments, one of which is illustrated in fig. 2, urine was tested for antidiuretic activity without extraction. In a preliminary experiment, in which urine flow and blood-pressure were measured simultaneously in a rat, it was found that a specimen of urine passed after smoking inhibited diuresis without causing any change in blood-pressure. The antidiuretic activity of the urine was abolished by treatment with sodium thioglycollate. It is concluded, therefore, that A.D.S. in untreated urine, as in extracts from urine, is identical with A.D.H., and that it acts independently of any effect on systemic blood-pressure. A.D.S. was detected in the urine in only one subject (1), and then only in specimens passed 30–105 minutes after commencement of smoking; the mean rate of excretion of A.D.S. during this period of 75 minutes was 0·98 milli-units per minute. Eisen and Lewis (1954), using a similar method of assay, found that the rate of excretion of A.D.S. in urine passed 15–60 minutes after smoking varied, in 9 individuals, from 0·08 to 3·0 milli-units per minute (mean, 1·1).

The antidiuretic responses and the amounts of A.D.S. excreted in the urine (subject 1) in the two experiments illustrated in figs. 1 and 2 were very similar. In the second experiment (fig. 2) the rate of excretion of A.D.S. in the urine 30–45 minutes after smoking had begun was 1·0 milli-units per minute. If it is assumed as before that the amount of hormone in the urine was 8·5% of that secreted, then the rate of secretion in this period was 11·8 milli-units per minute. Ginsburg and Heller (1953a) showed that when vasopressin is injected intravenously in the rat its disappearance from the circulation follows an exponential course with a half-life of 0·85 minutes. If the rate of secretion and the half-life of a hormone are known, it is possible by applying a simple exponential formula to calculate the maximum concentration attained in the blood; the maximum concentration is directly proportional to the half-life. The half-life for A.D.H. in man is unknown; but even if it were five times greater than that for vasopressin in the rat, then, given a rate of secretion of 11·8 milli-units per minute, the maximum concentration in the blood would be only 0·015 milli-units per ml. In the first experiment on subject 1, the level of A.D.S. in the blood 38 minutes after smoking had begun was found to be 0·007 milli-units per ml. It appears therefore that the levels of antidiuretic activity in the blood reported in this and previous work are not discordant with theoretical deductions.

In the experiment on subject 1 (fig. 2) it was observed that, at one point at which the inhibition of diuresis was at a maximum, the rate of excretion of A.D.S. in the urine was $<0·03$ milli-units per minute. From this it may be inferred that a rate of secretion of A.D.H. of $<0·3$ milli-units per minute is sufficient to cause maximal antidiuresis. It has, in fact, been shown by Barclay and Cooke (1950) that diuresis can be inhibited in man by the intravenous infusion of A.D.H. at a rate of 0·002 to 0·08 milliunits per minute. The low rate of excretion of A.D.S. during the latter part of the period of inhibition of diuresis explains the failure to detect antidiuretic activity in the blood of subject 3 105 minutes after cessation of smoking.

In subject 4, in whom only moderate inhibition of diuresis occurred, it is supposed that the amount of A.D.H. released was too small to be detected in either the blood or the urine. The failure to produce an antidiuretic effect by smoking in subjects 3 and 5, in one of whom a pronounced effect had been obtained in the previous series of experiments, illustrates a point on which Burn and Singh Grewal (1951) have commented—namely, the variability in response of different individuals to nicotine, and even of the same individual at different times. This may be of practical importance in diagnostic tests for diabetes insipidus in which nicotine is used to stimulate the neurohypophysis (Chalmers and Lewis 1951). Possibly in those individuals who do not respond to the antidiuretic effect of nicotine, release of A.D.H. from the neurohypophysis is inhibited by a high level of adrenaline in the circulation. A similar explanation has been given by Noble and Taylor (1953) in the case of individuals failing to excrete A.D.S. in the urine after stimulation of the neurohypophysis.

Effect of Amyl Nitrite on the Neurohypophysis

Brun et al. (1946) demonstrated that syncope, induced by tilting into the passive erect posture, was accompanied by inhibition of water diuresis. The antidiuretic effect was attributed, not to the transient changes in glomerular filtration-rate and renal blood-flow, but to increased tubular reabsorption of water due to release of A.D.H. from the neurohypophysis. It was thought that the induction of a rapid fall of blood-pressure might have a similar effect to that of syncope. The inhalation of amyl nitrite in subject 3 (fig. 3) did in fact cause inhibition of diuresis which lasted for 105 minutes, but antidiuretic activity could not be detected in either the blood or the urine. From the data of Burn and Singh Grewal (1951) it may be assumed that this inhibition was equivalent to the intravenous injection of about 100 milli-units pituitary (posterior lobe) extract. If 100 milli-units of A.D.H. were released into the blood-stream, it may be assumed that 8·5 milli-units would be excreted in the urine. But, even if the whole of this amount were excreted during the period of, say, 30 minutes following the inhalation of amyl nitrite the level in the urine would be approximately 0·1 milli-units per ml., and this approaches the limit of the assay method. Failure to detect antidiuretic activity in the blood at a level of 0·017 milli-units per ml. is in agreement with the observations of Brun et al. (1946). In one experiment these investigators withdrew 400 ml. of blood from a subject immediately after the induction of post syncopal oliguria which lasted for 90 minutes. When this blood was transfused into a second subject, during the course of water diuresis, inhibition was produced in the recipient for 30 minutes. From the data of Burn and Singh Grewal (1951) this would correspond with an injection of 3 milli-units of A.D.H., giving a concentration in 400 ml. of blood of 0·007 milli-units per ml.

Conclusion

It has been shown that, even when a powerful stimulus is applied to the neurohypophysis, and large amounts of an antidiuretic substance, which is believed to be identical with A.D.H., are excreted in the urine, the antidiuretic activity of the blood is so small that it can be detected

only in concentrated extracts. This reinforces our belief that the level of A.D.H. in the blood under normal conditions must necessarily be too low to detect by current methods of assay. Claims to have detected high levels of A.D.H. in human plasma or serum are invalidated by failure to use an intravenous assay technique.

It has been shown previously (Bisset and Lee 1957b, Lee and Bisset 1958) that it may be possible to detect antidiuretic activity in " central " blood (blood from the internal jugular vein) when activity is undetectable in " peripheral " blood. This suggests that, in order to study neurohypophysial secretion in pathological states, the use of " central " blood may be essential.

Summary

An attempt has been made to detect antidiuretic activity in the blood after stimulating the neurohypophysis by smoking cigarettes or inhaling amyl nitrite during water diuresis.

Antidiuretic substance (A.D.S.) in urine and in extracts from urine and blood was assayed against antidiuretic hormone (A.D.H.), with which it is believed to be identical.

In three experiments extracts were prepared from urine. The total amounts of A.D.S. excreted in the urine after smoking were 85, 57, and 259 milli-units, and the levels in blood from an arm vein, during or after smoking, were 0·007, 0·040, and 0·017 milli-units per ml. Activity was not detected in blood before smoking.

In the remaining experiments urine was tested without extraction, and rates of excretion of A.D.S. were measured at intervals of 15 minutes. In one experiment in which smoking caused profound inhibition of diuresis, the highest rate of excretion in the urine was 1·75 milli-units per minute. This occurred 45–60 minutes after smoking had begun. From 105 to 165 minutes, although diuresis was still almost completely inhibited, the rate of excretion of A.D.S. was less than 0·1 milli-units per minute.

From the quantity of A.D.S. in the urine the probable amount of A.D.H. secreted by the neurohypophysis was estimated. The theoretical level of A.D.H. in the blood was then compared with the observed level of antidiuretic activity.

Smoking did not inhibit diuresis in two experiments, and caused only moderate inhibition in a third. This illustrates the unreliability of nicotine or smoking as a test for neurohypophysial function.

Amyl nitrite, which was tested in one subject, caused only brief inhibition of diuresis. Antidiuretic activity was not detected in the blood or urine.

The results show that a strong stimulus to the neurohypophysis is required to produce detectable levels of antidiuretic activity in " peripheral " blood (blood from the extremities).

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LONG-TERM PROPHYLACTIC ADMINISTRATION OF TETRACYCLINE TO CHRONIC BRONCHITICS

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CHRONIC bronchitis is now the greatest problem in respiratory disease in this country (Fry 1954, Leese 1956). Its incidence is difficult to determine; but the disease is an important cause of disability and unemployment, being at least three times commoner in men than in women (Goodman et al. 1953). The ætiology is complex, including genetic and social factors and the effects of atmospheric pollution and tobacco smoking; but bacterial infection is widely accepted as playing a major role (Stuart-Harris et al. 1953, May and Oswald 1956). In addition to established bronchial infection, there are superimposed infections which characteristically punctuate the clinical course, may result in further permanent damage to the lung parenchyma (Reid 1954), and often present a hazard to life (Westlake 1954, 1955). Chemotherapy is generally considered to be more successful in the treatment of these exacerbations than in the eradication of chronic bronchial infection (*British Medical Journal* 1957). It has been repeatedly demonstrated, however, that antibiotics given over long periods produce clinical improvement in chronic non-tuberculous respiratory infections (McVey and Sprunt 1953, Helm et al. 1954, 1956, May and Oswald 1956, Medical Research Council 1957, Edwards et al. 1957, Moynes and Kershaw 1957).

The aim of the present trial was to ascertain whether long-continued tetracycline administration would reduce the incidence of acute exacerbations. This drug was used since it was found by Finland et al. (1954) to have fewer side-effects than either chlortetracycline (aureomycin) or oxytetracycline.

DR. BISSET, DR. LEE: REFERENCES—*continued*

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Method

The trial was conducted on male outpatients who attended for at least twelve months at three-weekly intervals. In all cases there was clear evidence of established chronic bronchitis, with persistent productive cough, undue effort dyspnœa, and a history of previous acute infective exacerbations, which in many cases had been treated in hospital. No patient had active tuberculosis and none had recently received antibiotic therapy.

Preliminary assessment consisted of a full history and clinical examination, X rays of chest and sinuses, electrocardiography, sputum culture, vital capacity determination, weight measurement, urinalysis, and full blood examination, including erythrocyte-sedimentation rate. The investigations were repeated at intervals during the trial. At intervals of six to twelve weeks, serum-tetracycline levels were estimated.

The patients were allotted by random selection to two groups: one group received tetracycline in a dose of 250 mg. night and morning; and the other group lactose in capsules of identical appearance. The clinicians alone knew which patients were receiving the active preparation. This method was preferred to the double-blind technique since, before the trial began, there had been reports of serious complications during the administration of such drugs—e.g., staphylococcal gastro-entero-colitis (Dearing and Heilman 1953, Hay and McKenzie 1954, Finland et al. 1954, Fowler 1955). Further, it was considered that the incidence of defined exacerbations would provide an adequately objective index of therapeutic effect.

TABLE I—NUMBERS OF TREATED PATIENTS AND CONTROLS WHO COMPLETED TRIAL AND WHO FELL OUT OF TRIAL

—	Treated group	Control group
Completed one year	21	15
Defaulted 5th–12th month	4	5
Defaulted 0–4th month	0	4
Died	1	1
Total	26	25

It was explained to family doctors that, while the trial was in progress, they might give any additional treatment considered necessary, apart from antibiotics. Consequently some patients received various preparations, such as sedative and expectorant cough mixtures, antispasmodics, and, when cardiac failure was present, digitalis and mersalyl.

After protracted administration of the tetracycline group of drugs, mucosal lesions resembling those associated with vitamin-B deficiency may develop (Goodman and Gilman 1955). Although administration of vitamin-B complex has been recognised as affording only variable relief, we considered it advisable to give all patients 1 g. of yeast daily.

51 patients were admitted to the trial: 26 received tetracycline and 25 the inert preparation. Of the 26 treated with the antibiotic, 21 completed the trial period of one year; 4 defaulted between the fifth and twelfth months; and 1 died. In the control group 15 patients completed one year in the trial; 5 defaulted between the fifth and twelfth months; 4 defaulted in the first four months; and 1 died. Thus 21 of the 26 treated patients and 15 of the 25 control patients completed the twelve-month-period of the trial (table I).

Both deaths were due to chronic cor pulmonale. The average age of the treated group was 61·1 years and of the control group 57·6 years.

Repeated bacteriological examination of the sputum was carried out in all cases except 9—5 of the 26 treated patients and 4 of the 25 controls. In all, a hundred and fifty-nine specimens from the treated group (21 patients) and a hundred and forty-five from the control group (21 patients) were examined.

Three culture plates were inoculated for each specimen: (1) horse-blood agar; (2) Fildes' peptic digest of blood-agar; (3) Fildes' plate screened with penicillin and streaked with a penicillin-resistant staphylococcus. Tetracycline discs containing 10 mg. and 100 mg. were applied to the unscreened Fildes' plate.

TABLE II—INCIDENCE OF MAJOR INFECTIVE EXACERBATIONS

—	Treated group (21)	Control group (15)
No. of patients with 0 exacerbations	14	5
" " " " 1 "	7	6
" " " " 2 "	0	2
" " " " 3 "	0	1
" " " " 4 "	0	1

Before the investigation started, twenty sputum samples were shaken with sterile glass beads in an attempt to break up tenacious material and cultured as above. They were then homogenised with pancreatin by the method of Rawlins (1953) and similarly cultured. In only one case was a pathogen not apparent on the first plate isolated after homogenising. The less time-consuming method was therefore used during the trial.

Ninety-seven estimations of serum-tetracycline were made on 19 patients in the treated group. Venous blood was withdrawn approximately two hours after ingestion of the morning dose of the drug. Initially estimations were made within two hours of withdrawal; but, since it was found that the levels were unaltered by storage at 4°C, specimens were occasionally kept for two or three days. Doubling dilutions in broth were made with both undiluted serum and serum diluted 1 in 10. The standard series was made from broth containing tetracycline 0·2 mg. per ml. The test organism was *Bacillus cereus* (National Collection of Type Cultures, no. 8035), and the inoculum was 1·5 ml. of 1 in 100 dilution of an eighteen-hour broth cu'ture. The tubes were incubated at 37°C in a water-bath for four hours and read immediately thereafter. The standard series gave a constant minimum inhibitory concentration of 0·025 mg. per ml.

Results

For the purpose of the trial, acute infective relapses were defined as severe exacerbations of the bronchitic state requiring the patient to remain in bed for at least five days. The frequency of such relapses in the treated and control groups is shown in table II.

The cases treated for the full trial period of a year are considered separately, since those treated for a shorter period are not strictly comparable with one another or with the main group.

Of the 21 cases treated for a year, 14 had no exacerbations and 7 had one exacerbation, giving a mean of 0·33 exacerbations per patient per year. Of the 15 control cases, 5 had no exacerbations, 6 had one, 2 had two, 1 had three, and 1 had four. Thus 15 patients in this group had a total of seventeen exacerbations, giving a mean of 1·13 exacerbations per patient per year. The two frequency distributions agree very well with two Poisson distributions. On this basis the difference in incidence of exacerbations is highly significant ($0·01 > P > 0·001$).

TABLE III—SUMMARY OF BACTERIOLOGICAL FINDINGS ON SPUTUM EXAMINATION IN CHRONIC BRONCHITICS RECEIVING EITHER TETRACYCLINE OR AN INERT PREPARATION

Group	No. of patients					
	Total	Pathogens isolated				No pathogens isolated
		H. influenzæ	Pneumococci	Friedländer's bacillus	*Staph. pyogenes*	
Untreated	21	17	8	2	2	2
Treated, producing:	21					
Mucus only	13	2	2	1	0	8
Persistent mucopus	2	2	0	1	1	0
Occasional mucopus	6	6	0	0	1	0

In the smaller subsidiary group treated for less than a year, a similar trend was observed.

There were no serious complications which could be attributed to the administration of tetracycline. Minor upsets, however, did occur: 1 patient had diarrhœa, which responded to temporary withdrawal of the drug; while another complained of abdominal pain and defaulted during the early stage of the trial.

No notable changes were observed, during the trial, in the treated or in the control group on physical examination, serial chest radiography, vital-capacity determinations, hæmoglobin level, packed-cell volumes, or erythrocyte-sedimentation rates. The only significant electrocardiographic change was the development of right bundle-branch block in the tracings of 1 control subject. Subjectively, however, the treated group appeared to be improved, with a reduction in cough and the volume and purulence of sputum. 15 of the 21 treated patients gained weight, compared with 6 of the 15 controls.

Bacteriology

In the 21 controls *Hæmophilus influenzæ* was isolated from the sputum of 17, pneumococci from 8, Friedländer's bacillus from 2, and *Staphylococcus pyogenes* from 2. No pathogens were isolated in 2 cases, although nine specimens of sputum from 1 of those patients and three specimens from the other were examined. In this group 19 patients produced persistent or recurrent mucopus; 2 produced mucus only, but 1 of these yielded a profuse growth of *H. influenzæ*.

TABLE IV—SERUM-TETRACYCLINE LEVELS IN CHRONIC BRONCHITICS RELATED TO CHARACTER OF SPUTUM

Sputum	No. of patients	No. of estimations	Serum level (μg. per ml.)		
			>1·0	0·5	<0·5
Persistent mucopus	2	9	4	2	3
Variable sputum	6	25	13	9	3
Persistent mucus..	11	67	32	24	11

13 of the 21 patients who were treated with tetracycline produced mucus only. Soon after treatment was begun, *H. influenzæ* was isolated from 2 and pneumococci from another 2 of these 13—each once only. Friedländer's bacillus was grown from 1 patient's sputum after five months' therapy.

The remaining 8 treated patients produced persistent or intermittent mucopus. 2 produced persistent mucopus from which *H. influenzæ* was frequently cultured, Friedländer's bacillus once, and tetracycline-resistant *Staph. pyogenes* once. The remaining 6 patients in this group produced sputum which was occasionally mucopurulent, and *H. influenzæ* was isolated once or at most twice from each. In 1 case tetracycline-resistant *Staph. pyogenes* was grown. In these 8 patients the only notable change in the bacterial flora under the influence of tetracycline was the disappearance of pneumococci. These results are summarised in table III.

Coliform organisms grew profusely on culture of sputa from both treated and control patients, but were commoner in the tetracycline group: they were observed in fifty-eight out of a hundred and fifty-nine specimens from treated patients, compared with thirteen out of a hundred and forty-five specimens from controls. Heavy growths of yeasts were very infrequent, and occurred in only seven of the hundred and fifty-nine sputa from patients receiving tetracycline and in three of the hundred and forty-five controls.

TABLE V—SERUM-TETRACYCLINE LEVELS IN TREATED GROUP

Serum levels (μg. per ml.)	No. of estimations
<0·4	2
0·4–0·5	13
0·8–1·0	36
1·2–1·6	20
2·0	22
4·0	4

The application of discs containing tetracycline to a sputum-inoculated plate gives a reasonably clear indication of tetracycline sensitivity only when a pathogen predominates. Where such a growth occurred, no resistant strains of *H. influenzæ*, pneumococci, or Friedländer's bacilli were found. The two strains of *Staph. pyogenes* obtained from controls were sensitive to tetracycline. Both strains isolated from the treated patients were resistant: in each case the organism was cultured only once.

Ninety-seven estimations of the serum-tetracycline level were made during the trial. The level varied between 0·1 and 4·0 μg. per ml.; but the lower levels were uncommon (table V). The mean of the estimations was 1·345 μg. per ml. It was not possible in individual cases to demonstrate any correlation between serum-tetracycline levels and responses to treatment, judged by the naked-eye appearance of the sputum (table IV).

At the end of the trial the anterior nares of the 21 treated patients were swabbed, and *Staph. pyogenes* was obtained from 3 (14%). These organisms were resistant to tetracycline.

Discussion

Since infection is commonly associated with exacerbation of chronic bronchitis, its prevention or control seems a rational measure in the management of patients with this disease. It has been shown that short courses of penicillin, chlortetracycline, chloramphenicol, and sulphadimidine fail in this respect (Elmes et al. 1953), while a triple sulphonamide or autogenous *H. influenzæ* vaccine has little or no value (Edwards et al. 1957). Long-continued therapy with wide-spectrum antibiotics has yielded more promising results, and Edwards et al. (1957) have also confirmed that oxytetracycline used in this way confers sustained clinical improvement and reduces the number of exacerbations. Although chloramphenicol controls or eradicates *H. influenzæ*, which often predominates in bronchitic sputum, it is contra-indicated as a drug for protracted administration, owing to the danger of blood dyscrasia (Franklin and Garrod 1953).

In the present study we have observed that tetracycline, administered over long periods to male chronic bronchitics can reduce the incidence of acute exacerbations. This might be attributed to a reduction in the number of head colds, which are especially common in chronic bronchitics and which result in increased cough and sputum (Leese 1956). May and Oswald (1956) stressed that when tetracycline or oxytetracycline is given to chronic bronchitics over long periods, the frequent head colds do not result in worsening of the bronchitic state. During the present trial this observation was confirmed.

Wide-spectrum antibiotics can considerably reduce the incidence of *H. influenzæ* and pneumococci, both common pathogens, in bronchitic sputum, though without necessarily suppressing the organisms completely. These drugs can produce clinical improvement and reduce the incidence of exacerbations in chronic bronchitis (McVey and Sprunt 1953, Helm et al. 1954, 1956, May and Oswald

1956, Edwards et al. 1957, Medical Research Council 1957). Although we were unable to demonstrate in our treated patients notable improvement, judged by clinical examination, electrocardiography, X-ray and blood examination, these patients did feel better during therapy, and produced less purulent sputum. Further, we clearly demonstrated a significant reduction in the number of exacerbations.

The bacterial flora in the sputum of the 21 controls conformed to a pattern of pathogen isolation not infrequently described, especially in the emphasis on the predominance of *H. influenzæ* (Stuart-Harris et al. 1953). These findings in total sputum samples were confirmed by Brumfitt et al. (1957); but they suggested that the pneumococci were contaminants from the throat in most instances. In our small group of treated subjects who produced mucopurulent sputum, tetracycline-sensitive *H. influenzæ* persisted, whereas pneumococci disappeared. Although we did not obtain confirmatory bronchoscopic evidence, it is possible that in our cases also the pneumococci came predominantly from the throat, and that the antibiotic acted mainly on organisms in the upper respiratory tract rather than those in the bronchial tree. This conjecture would accord with the suggestion of Edwards et al. (1957) that the value of the antibiotic might lie in the prevention of bronchial superinfection from an infected upper respiratory tract, rather than in direct action on the established bronchial flora, since they had noted a discrepancy between failure to eradicate pathogens from the sputum and the conferring of clinical benefit.

An alternative explanation is that the bronchial bacterial flora might be dormant, in which case antibiotics might have relatively little effect (*British Medical Journal* 1957); but it is also possible that the dose of antibiotic was suboptimal, although demonstrably effective in reducing the incidence of exacerbations.

General agreement on the minimum therapeutic serum level of tetracycline has not yet been reached; but F. R. Fletcher (personal communication) suggests that it is not greater than 0·687 μg. per ml. In the present series, the mean serum level was 1·345 μg. per ml. Levels exceeding Fletcher's figure were observed at some time in every case, and on only 15 occasions were lower levels observed. It was not possible to demonstrate a correlation between the serum tetracycline level, alteration in the bacterial flora of the sputum, or clinical progress.

No tetracycline-resistant strains of *H. influenzæ* emerged during the trial, and at its conclusion only 3 patients (14%) harboured coagulase-positive tetracycline-resistant staphylococci in their anterior nares. Unfortunately we did not undertake a full survey of the incidence of nasal carriers of staphylococci during the trial, and the number of patients harbouring the organisms in their nares before treatment is unknown. No information therefore is available regarding the emergence of tetracycline-resistant organisms; but the final prevalence compares favourably with that noted by May and Oswald (1956), who recorded a carrier-rate of 25%. As these workers indicate, this is an alarming figure; but it is in keeping with the incidence of antibiotic-resistant staphylococcal carrier-rate in hospital patients as a whole (Barber and Burston 1955).

Since all patients admitted to the present trial lived in the same area of Glasgow and were observed during the same period, such environmental factors as climate and locus influenced both groups equally. At the beginning of the trial the same proportion of each group was employed (28%). In the treated group 1 patient who had been unemployed for some years because of his disability from bronchitis felt well enough to resume regular light work. There were more defaulters in the control group (10 out of 25) than in the treated group (5 out of 26) (table I). Possibly dissatisfaction with the treatment or increased disability were factors resulting in failure to attend.

There is a strong clinical impression that tetracycline and the related antibiotics are of value in the management of the chronic bronchitic patient; our results confirm this. Although tetracycline is expensive, against its cost must be set the considerable reduction in the use of expensive hospital beds for the treatment of exacerbations and an increase in the working-time and earning capacity of chronic bronchitics. Further, each exacerbation represents a hazard to the patient's life, and any measure which reduces this hazard should be considered seriously and not rejected summarily on the ground of cost. Prophylactic antibiotic therapy in only the winter months would reduce the cost of treatment; but workers employing this regime have not reported the results of treating their cases in subsequent winters, although the benefit conferred by six months' continuous antibiotic therapy was significant. A relatively small dosage of tetracycline not only reduces the cost of therapy but also apparently decreases the likelihood of serious side-effects. Although the most effective drug regimen has not yet been established, we can conclude from the present trial that long-term administration of tetracycline 250 mg. twice daily is an effective prophylactic against potentially lethal acute exacerbations, and is indicated in the treatment of chronic bronchitis.

Summary

Tetracycline 250 mg. twice daily was given to 26 male outpatients with chronic bronchitis. A control group of 25 similar patients received an inert preparation of identical appearance.

In the treated group there was a statistically significant reduction in the number of exacerbations, compared with the control group.

Subjectively the treated patients were improved and had less cough, with reduction in the volume and purulence of the sputum. More of them gained weight than of the controls. No improvement was found on objective investigation.

There were no serious side-effects attributable to tetracycline. Satisfactory serum-tetracycline levels were obtained.

This form of therapy is indicated in the long-term management of chronic bronchitis.

We wish to thank Dr. L. D. W. Scott for permission to study these cases and for helpful encouragement; Dr. F. R. Fletcher, of Messrs. Pfizer, for supplies of 'Tetracyn' and control tablets; and the nursing staff of the outpatient department of the Southern General Hospital; in particular we are indebted to the late Sister Jane Kennedy, for helpful cooperation. We are specially indebted to Dr. J. B. de V. Weir, who undertook the statistical analysis.

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EFFECTS OF ISOPRENALINE ISOMERS IN MAN

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IT has been claimed (Schmidt and von Stackelberg 1954) that for a given bronchodilator effect the *l*-isomer of isoprenaline causes less palpitation and restlessness than does the racemic mixture, and is therefore to be preferred in the treatment of asthma. This claim is surprising in view of animal work suggesting that *d*-isoprenaline is relatively inactive (Lands et al. 1954), but the effects on man of the two isomers do not appear to have been directly compared. This paper reports such a comparison.

Methods

The experiments were performed on three medical students, two men and a woman, aged 22–26. The arterial blood-pressure was continuously recorded by means of a needle in the brachial artery attached to a capacitance manometer. Vascular resistance in the arm was estimated by the "arterial run-off" method of Hayter and Sharpey-Schafer (1958). Respiratory movements were recorded by means of a pneumograph giving a deflection proportional to the tidal air (Dornhorst and Leathart 1952). Subjective effects were reported and compared.

A steady intravenous infusion of saline solution was set up, using a mechanically driven syringe. After a control period, the freshly diluted test solution was substituted without the subject's being aware of it. Each test solution was infused for 3 to 5 minutes and it was followed by approximately 5 minutes of saline solution; at the end of this time the effects of the drug had worn off. Usually the two isomers were given alternately and each was given at least two dose levels.

The product of the heart-rate and the pulse-pressure has been used to assess the general circulatory effect, the increase in the product being plotted against the dose of the drug. For respiratory effects the pneumograph deflections, summed over 30 seconds, were similarly plotted. The reciprocal of the resistance index of Hayter and Sharpey-Schafer was used to estimate dilatation of the arm vessels.

Results

The slopes of the dose-effect lines for the circulatory product agree satisfactorily, and the results indicate that the *l*-isomer is just under fifty times as potent as the *d*-isomer (fig. 1). Similar results were obtained for respiratory and peripheral dilator effects in two of the subjects, but in the third (the woman) the measurements suggested a lower activity ratio.

The subjective effects corresponded well with the objective measurements.

The local effects of the two isomers when injected intradermally in comparable doses in three normal subjects were qualitatively similar. Each produced a central pale area surrounded by a flare, as has been previously described for the racemic form (Herxheimer 1956).

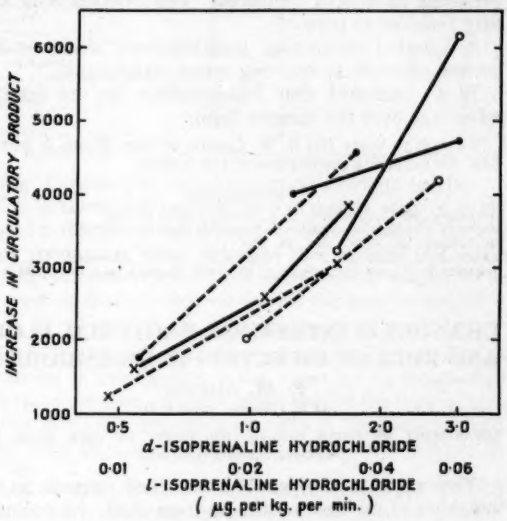

Fig. 1—Effects of *d*-isoprenaline (continuous line) and *l*-isoprenaline (interrupted line) on circulation. Increase in product of heart-rate and pulse-pressure has been plotted against dose. Subjects are represented by different symbols.

Discussion

The results show that our specimens of *d*-isoprenaline had only about one-fiftieth the circulatory activity of the *l*-isomer. This represents a minimum ratio since complete separation of the two isomers is technically difficult, and the dextro solution almost certainly contained some lævo. But even accepting this ratio, it is clear that the *d*-isomer in a racemic mixture will contribute negligibly to the circulatory effects.

It might still be desirable to exclude the dextro form if it interfered with the bronchodilator action of the lævo. To exclude this possibility a suitable dose of our dextro solution was injected subcutaneously in a patient in status

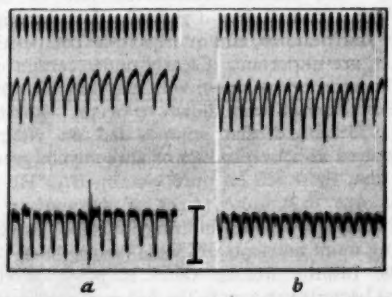

Fig. 2—Pneumograph (above) and intrathoracic pressure in status asthmaticus, (a) immediately before and (b) 4 minutes after subcutaneous injection of 10 mg. *d*-isoprenaline. Time marked in seconds: pressure standard is 30 mm. Hg.

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asthmaticus. A clear-cut bronchodilator effect was produced (fig. 2).

In view of these findings we suggest that the pharmaceutical separation of the isoprenaline isomers has no advantage to justify the cost entailed.

Summary

Circulatory and respiratory activities of *d*- and *l*-isoprenaline have been compared. The *l*-isomer is at least fifty times more potent.

A solution containing predominantly *d*-isoprenaline proved effective in relieving status asthmaticus.

It is concluded that *l*-isoprenaline has no material advantage over the racemic form.

We wish to thank Dr. B. W. Cromie of John Wyeth & Brother Ltd., for supplying preparations of the isomers.

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CHANGES IN INTESTINAL BACTERIAL FLORA AND ROLE OF INFECTION IN KWASHIORKOR

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THE exact part played by intestinal bacteria in the nutrition of the host is still far from clear. Nevertheless certain broad concepts have emerged:

Firstly, that the diet can determine the pattern of the bacterial flora is shown by Györgi's (1953) work on the breast-milk factor in establishing the predominance of *Lactobacillus bifidus* in the human infant's fæces.

Secondly, that bacteria can synthesise vitamins is shown by the high concentration of vitamin B_{12} in cowdung, and also by the habit of refection whereby animals synthesise and absorb some of the B vitamins from their digestive tracts (Fridericia et al. 1928).

Thirdly, that bacteria metabolise vitamins is shown by the necessity of enriching culture-media in order to obtain optimal growth.

Lastly, some mechanism must come into play that limits the growth of bacteria in the intestine. Their tremendous potential growth is shown by the fact that under optimum conditions coliform bacilli can divide every twenty to thirty minutes (Perret 1952). In twenty-four hours two bacilli could have increased to 2^{48}—which is about 280 billion bacilli, the nutrient and vitamin requirements of which would be about those of a 28 lb. infant.

Exactly what factors control the rate of bacterial growth is not known, but it is likely that the supply of nutrients and vitamins, and interbacterial competition and inhibition, are important. Clearly under certain circumstances bacteria can compete with the host for nutrients; in animals this has been shown to occur. Stokstad and Jukes (1950) found that animals fed on vitamin B_{12} manufactured as a by-product of aureomycin grew more rapidly than those fed on pure vitamin B_{12}. He showed this was due to minute traces of aureomycin in the commercial preparation inhibiting intestinal bacteria and so making more nutrients available for the host.

In the healthy human there is evidence that the intestinal bacteria can satisfy the full requirements of only biotin and vitamin K (Mickelson 1956). Little is known about their part in disease, although it has been suggested that the intestinal bacteria are an important factor in the development of the deficiency states associated with the loop and stagnation syndromes of the small bowel (Brown 1949); in the megaloblastic anæmia which can be cured by giving penicillin (Foy et al. 1951); and in hepatic coma where improvement follows the administration of intestinal antibiotics (Dawson et al. 1957).

By applying these principles to kwashiorkor it is not unreasonable to postulate that the protein-deficient diet disturbs, not only the nutrition of the child, but also the intestinal bacterial pattern and the degree of bacterial growth. Possibly by spreading to the small bowel these bacteria cause diarrhœa, compete with the host for nutrients and vitamins, and liberate toxins, which in the presence of disturbed liver function contribute to the clinical picture of the disease.

If this hypothesis is correct it should be possible to improve on the present treatment by altering the intestinal flora. This I have attempted by first sterilising the bowel as far as possible with antibiotics, and then seeding it with what were thought to be desirable bacteria found in yogurt.

There is still a considerable mortality from kwashiorkor. During the past three years 97 (45%) of 213 cases admitted to this hospital died. No less than half of these died in the first forty-eight hours; if they are excluded the mortality is 23%. There has been a tendency to assume these early deaths are inevitable—that these children have gone beyond the point of no return from malnutrition. If they have reached a critical level, it might be supposed that inhibition of intestinal bacteria with their nutritional demands might help to reverse the downward course sooner and so decrease the mortality. There is, however, evidence that many of these deaths are due to infection. Suckling (1955) first stressed the need for routine antibiotic cover against infection. This routine prophylaxis was subsequently used by Brock et al. (1955) in their trials. Campbell (1956), having studied the necropsy material from this hospital, laid particular emphasis on the importance of infection, which he considered the major cause of death. It seems desirable, therefore, that the part played by overt infection, and the effect of giving greater emphasis to its treatment in kwashiorkor, should also be reviewed.

Method

33 consecutive cases which fulfilled the diagnostic criteria of kwashiorkor laid down by Brock and Autret (1952) were investigated. All the patients were moderately or severely ill, as, owing to the pressure on bed-space, mild cases cannot be admitted. Only tuberculous infections were excluded. Routine clinical and laboratory examinations were carried out in most cases. These included urine analysis, chest X-ray, Mantoux test, weekly estimations of serum-proteins, bone-marrow studies, rectal swab on admission and after three days of antibiotic therapy, bacteriological examination and pH of stomach contents, and blood-culture on admission and immediately after death.

Treatment

Both chloramphenicol and neomycin in doses of 40 mg. per lb. body-weight per day were given in divided doses three-hourly for three days. Nystatin 100,000 units t.d.s. was added to inhibit fungi. From the fourth day intramuscular penicillin and streptomycin were given if active infection persisted, except in 5 cases with salmonella or staphylococcal infections in which chloramphenicol was given for a longer period.

All "feeds" were made up to a standard volume/body-weight ratio of $2^1/_2$ oz. per lb. per day, given by bottle or stomach tube if the child refused to drink. For the first day half-strength Darrow's solution and 5% glucose solution were given; skimmed lactic acid milk (S.L.A.M.) for the next two days;

equal parts of S.L.A.M. and yogurt for three days; and by the tenth day a diet which consisted of milk and 'Nutrine' for the younger children, with added eggs, mince, fish, and vegetables for the older ones. 1 g. of potassium chloride daily was added for the first week. 'Vi-daylin' 1 drachm b.d. was given routinely, and extra vitamins were added if any specific deficiency was present. The yogurt contained *Lactobacillus bulgariensis* and was obtained from the local dairy.

Results

Among 33 cases there were 5 deaths—a mortality of 15%. Excluding the 2 deaths within forty-eight hours of admission, the mortality is 9%. 3 children died of overwhelming infection; 1 had gangrene of the eyelid and vulva, megaloblastic anæmia, and a terminal *Pseudomonas aeruginosa* septicæmia; 1 had lobar pneumonia, pneumococcal and *Salmonella typhimurium* septicæmia, and rickets; the 3rd had cancrum oris, a paracolon septicæmia, and features that corresponded with the changes in the so-called "nutritional" heart.

The heart was enlarged, weighing 52 g. All chambers were dilated and the left ventricle was much hypertrophied. The muscle was shiny and in places almost translucent; microscopy showed alteration in size of muscle-fibres with intracellular and intercellular œdema and capillary congestion.

2 patients died unexpectedly; one had purulent otitis media and what appeared to be cellulitis of the leg, while the other was marasmic and had gross muscular wasting. At necropsy no satisfactory cause of death was found in either case, although there was cardiac dilatation in the 2nd, and both had areas of gross œdema of the large bowel.

Of the remaining 28 patients, 1 had *Staphylococcus aureus* septicæmia and recovered; 7 had clinical and radiographic evidence of pneumonia; 6 had otitis media; 3 had salmonella, 3 shigella and 2 ascaris infection; 1 had a megaloblastic bone-marrow. 16 out of 20 had a gastric pH of 4·5 or less; 3 with a pH of 7 had altered blood and mucus in the aspirate, suggesting gastritis. In two-thirds of all cases there was evidence of some active bacterial infection.

The accompanying table shows the result of culturing the gastric juice and fæces on admission, and the frequency with which the same organism was cultured from both sites. After three days of antibiotics 17 out of 20 children that were tested had scanty or no growth from the rectal swab; in the remaining 3 there was only a moderate growth of bacteria. *Ps. aeruginosa* was the commonest organism to persist despite the antibiotic therapy.

BACTERIAL GROWTH FROM GASTRIC JUICE, AND RECTAL SWAB, AND EFFECT OF THREE DAYS' ANTIBIOTIC TREATMENT ON THE INTESTINAL FLORA, IN 20 PATIENTS WITH KWASHIORKOR

Organisms	Gastric juice	Rectal swab	Both gastric juice and rectal swab	Rectal swab after 3 days' antibiotics
Staph. aureus	10	8	6	0
Coliforms	11	17	11	5
Salmonella	1	3	1	1
Shigella flexneri	0	2	0	0
Paracolon	2	5	1	4
Enterococci	0	4	0	7
Proteus morgani	0	14	0	4
Ps. aeruginosa	0	0	0	6
Extent of bacterial growth:				
None	3	0	..	5
Scanty	10	0	..	12
Moderate	6	0	..	3
Heavy	1	20	..	0

Fig. 1 shows the rise in the serum-albumin levels.

Fig. 2 shows the loss and gain in weight relative to the day of minimum weight, which is charted as day 0. The days preceding this indicate the number of days during which there was loss of weight due to œdema. The succeeding days are charted against the gain in weight.

Criteria of Severity

One of the difficulties in comparing the results of treatment of kwashiorkor is that there are no satisfactory criteria of severity. To give some idea of the type of case in this series the frequency of some of the factors which have been thought to affect the prognosis adversely is set out:

Age.—4 (12%) children were less than 6 months old; 8 (24%) were in the 6–12-month age-group; 8 (24%) 12-18 months; 7 (21%) 18–24 months; and 6 (18%) over 2 years of age. 1 child that died was 5 months old; the remaining 4 were all over 18 months.

Marasmus.—Comparing minimum weight with the mean for American boys and girls of similar age (Nelson 1954) 1 child (3%) was less than 40% of his expected weight; 7 (21%) were between 40% and 50%; 13 (39%) between 50% and 60%; 8 (24%) between 60% and 75%; and 4 (12%) were over 75%. Deaths occurred in children who weighed 42%, 45%, 75%, 78%, and 82% of their expected weight. As they were all still œdematous, this would not truly reflect their degree of undernutrition.

Anorexia of sufficient severity to necessitate tube feeding was present in 13 cases (40%). It occurred in 3 out of the 5 children who died.

Infection.—Undoubtedly the factor which most seriously affected the prognosis was infection. Septicæmia or infective gangrene was present in 3 of the 5 children that died, and

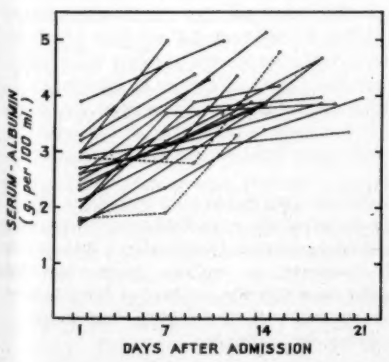

Fig. 1—Rise of serum-albumin during treatment of kwashiorkor; and delay in rise in 2 cases with severe infection (dotted line).

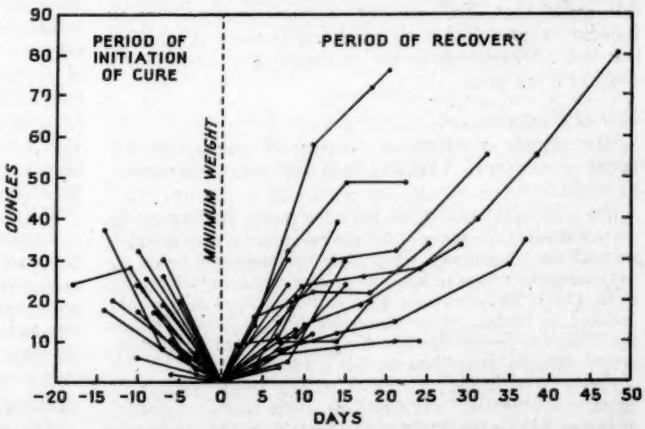

Fig. 2—Loss of weight during period of initiation of cure, and subsequent gain in weight during period of recovery.

among those that recovered it was infection that caused the most concern.

Diarrhœa and electrolyte disturbances did not affect the prognosis, possibly because of the rapid response of the diarrhœa to treatment and the early administration of extra potassium.

Apart from emphasising the importance of infection, this confirms the unsatisfactory nature of the criteria of severity in kwashiorkor and the difficulty in comparing mortality-rates. Even with a control series, unless of considerable size, the validity of any comparisons seems doubtful until some better criteria are defined.

In an attempt to find other criteria, loss of muscular power was estimated. There is little doubt that in protein malnutrition voluntary muscle is the depot from which protein is withdrawn, and the degree of wasting should be a good criterion of the severity of protein lack. Muscle bulk cannot be estimated directly, but the loss of muscular power should be some reflection of the loss of muscle bulk. Children were tested by being pulled up by their arms from a lying to a sitting posture. No conscious normal child over about the age of 4 months will fail to make every effort to pull its head forward when this is done and to prevent it flopping back when the child is laid down. (The head must be protected from falling back too violently.) Weakness may be accentuated by potassium lack, so the test was repeated forty-eight hours after the initial potassium therapy. Other factors, such as infection, may contribute to the muscular weakness and should be taken into account when interpreting the findings. 11 patients in this series were too weak to pull up their heads.

Subsequently, and, unfortunately too late for all the children to be tested, three grades of muscular weakness were defined:

Grade I was the state in which muscular wasting was present but the effects of gravity could be overcome. The child could sit and pull up its head.

Grade II, in which gravity could not be overcome, was most easily demonstrated by inability to pull up the weight of the head. The head could be supported when sitting erect.

Grade III was one of complete muscular atonia. The head flopped in any direction, the legs were immobile, and lastly even movements of the hands ceased.

Of the 5 children that died, 4 were in grade III. 3 of these had severe infection.

Another possible criterion which is under investigation is wasting of heart-muscle and the role of the heart in the cases of sudden death in kwashiorkor. 2 children in this series that died suddenly and unexpectedly were thought to have died from a cardiac cause—a possibility that was strengthened by the finding of a " nutritional " heart in a 3rd case.

Rate of Recovery

The efficacy of treatment can also be assessed by the speed of recovery. This has been expressed in a variety of ways:

The serum albumin.—It has not been shown that the rise in the serum-albumin varies sufficiently to make it a satisfactory method for comparison, while high serum-protein levels do not necessarily reflect an adequate level of nutrition (Scrimshaw et al. 1951). Failure of the serum-albumin level to rise may indicate an inadequate or unsuitable protein intake, but, as fig. 1 shows, severe infection can also delay the rise of the serum-albumin, even when the diet is adequate.

Period of initiation of cure.—This has been defined by Brock et al. (1955) as " the period when skin lesions are healing or healed, œdema has subsided, and there is a definite improvement in appetite and mentality ". Entirely suitable as this definition was for the purpose of that particular investigation the end-point was indefinite. A more clearly defined end-point (see fig. 2) can be obtained by taking the number of days' treatment required until the minimum weight is reached, after which there is a sustained rise in weight which is not due to œdema. Judged by this standard, the average period of initiation of cure in this series was eight days. In all children with severe infection the period was longer than eight days.

Gain in weight.—This was measured from the day of minimum weight (see fig. 2)—that is after completion of the period of initiation of cure. The average gain was 1·66 oz. per day with a total gain of 788 oz. during 474 hospital days. The maximum increase was 95 oz. in 22 days.

Discussion

Admittedly the method of defining the periods of initiation of cure and recovery (fig. 2) has certain defects. A few children gained weight from the time of admission, presumably because of some adjustment between intracellular and extracellular fluid. Some patients appeared slightly dehydrated at the time of diuresis, and this may have exaggerated their subsequent gain. The amount of dehydration is, however, likely to be small, and the sustained rise in weight indicates that it is not an important factor.

There is little reported information about weight gain in kwashiorkor. Allison (1951) by feeding different proteins to growing puppies showed that weight gain does not necessarily reflect nitrogen retention. It would be helpful to know the value of weight gain after protein malnutrition had first produced in puppies a kwashiorkor-like picture. There is little doubt that weight gain is an excellent criterion of how a child is thriving, and it has the advantage of simplicity. It could be used to follow large series over long periods, which would reduce the influence of individual variation. Furthermore, by measuring weight gain during the recovery period, the complicating effects of infection and possibly disturbed intestinal flora would be largely eliminated.

Significance of Infection

This series of cases has confirmed Campbell's (1956) findings on the extent to which kwashiorkor in Cape Town is complicated by infection. The high incidence of septicæmia was particularly striking. The fact that in 3 cases intestinal organisms were grown on blood-culture raises the possibility of increased susceptibility of the bowel wall to invasion by bacteria. Œdema of the bowel wall, seen in 2 cases, might predispose to such an invasion. Infection was an important cause of death, and severe infection delayed the rise in the serum-proteins and prolonged the period of initiation of cure. Lesser degrees may have had an effect that was not readily detectable. It would be surprising if infection did not play a part in kwashiorkor, since it has been shown to lower the serum-proteins despite adequate protein intake (McNaught et al. 1936); it can inhibit the formation of pancreatic enzymes (Véghelyi 1949); it can cause a fatty liver; it can raise the serum-globulin and cause fluid retention (Rutstein et al. 1945).

So prominent was the part apparently played by infection that it might seem that the improved results were due solely to the use of more powerful antibiotics. It does not seem reasonable, however, to exclude from any trial infected cases (apart from the tuberculous) as there can be all grades of severity, and even to establish that no infection is present can be very difficult.

The Intestinal Bacteria

The gastric contents were examined in an attempt to show the spread of bacteria up the intestinal tract. In

only 2 cases were the findings possibly significant—when a salmonella and *Ps. aeruginosa* were recovered from both gastric juice and stool. The presence of coliform organisms in the stomach in 11 cases cannot be taken as evidence of an upward spread, as they may be present in health. But this could be a significant finding if excessive growth of normal inhabitants of the bowel play a part in the disease. Intubation of the small bowel is more likely to be informative and is being attempted. Spread of bacteria up into the small bowel is suggested by the not-infrequent demonstration of dilated loops and fluid levels on X-ray examination, the recognised association of small-bowel dysfunction with deficiency states, and also the watery type of diarrhœa. In only a few cases did the stools show a cellular exudate or pus such as is found in infections of the large bowel. Although the stools in the diarrhœa of kwashiorkor are usually copious and swarming with bacilli, proof of an increase in numbers is obviously difficult; but Gordon et al. (1957) found that feeding excessive numbers of even such desirable bacteria as the *Lactobacillus acidophilus* provoked diarrhœa. They also suggested that the bad effects of sugar on diarrhœa could be due to its nutritive effects on the intestinal bacteria. In kwashiorkor the intolerance to some foods is possibly due to their effect on the intestinal bacteria.

There is little doubt that the rapidity of recovery in this series was influenced by the speed at which the diarrhœa improved and at which a full diet could be established without any relapse. In only 2 cases was diarrhœa not present on admission; in most it was severe with frequent watery or pultaceous stools. By the third day of antibiotic treatment the stools had become yellow and often looked gelatinous with a fair amount of mucus and fluid. It was after stopping the antibiotics and commencing the yogurt that the stools (sometimes within twenty-four hours and nearly always within three days) became yellow and formed or semiformed. So effective was the treatment that subsequently it was used with success for resistant cases of gastroenteritis. A controlled trial is at present being conducted in gastroenteritis from which it is hoped to determine the exact part played by the yogurt.

No claim is made for yogurt. Equally good results might have been obtained with ordinary milk, with which a normal intestinal flora might still have been established much as happens in a newborn infant born with a sterile intestinal tract. Yogurt was used partly with the idea that a more desirable flora could be more rapidly established and so help the diarrhœa, and partly to prevent staphylococcal enterocolitis in an intestine cleared of other bacteria.

Certain clinical features of kwashiorkor, which have never been satisfactorily explained, may be due to disturbed intestinal bacterial pattern. The way in which the full-blown syndrome is often ushered in quite suddenly with anorexia and diarrhœa, when the diet has not been changed for weeks, may be due to the effect of overgrowth of intestinal bacteria and toxæmia superimposed on protein insufficiency. The regularity with which kwashiorkor and the gastroenteritis season overlap may be due, not only to the loss of nutrients associated with the diarrhœa, but also to bacterial changes. Quantitative or qualitative alteration in the bacteria that synthesise or metabolise vitamins and aminoacids may account for the striking variation in the severity and rapidity of appearance of the dermatosis, cheilosis, purpura, and megaloblastic anæmia in different cases in which the patients are on essentially the same diet. Re-establishment of normal vitamin-synthesising bacteria may explain the healing of lesions while children are on a vitamin-free diet. Environmental effects on the bacterial pattern may explain the high incidence of megaloblastic anæmia in Durban and the fairly low incidence in Pretoria, when maize is the main source of diet in both places. Differences in the type of carbohydrate may also effect the flora. Uganda kwashiorkor on a banana diet may be different from Cape Town kwashiorkor on a diet of squashes. In fact diarrhœa seems to be less severe in Uganda and less of a problem in treatment. In occasional cases there is no diarrhœa; possibly these are the only cases of protein malnutrition which are uncomplicated by any severe disturbance of the intestinal bacteria.

There is no suggestion that the fundamental ætiological factor in kwashiorkor is other than a protein-deficient diet. What is being suggested is that a child on a protein deficient diet may be precipitated into the syndrome of kwashiorkor either by overt infection or by a disturbance of the intestinal floral pattern, or by both, and that the least common form of the disease seen in Cape Town is a pure protein malnutrition uncomplicated by either of these factors.

Summary

It is suggested that one effect of an inadequate protein diet is disturbance of the intestinal flora, and that this plays a significant part in the clinical picture of kwashiorkor.

In 33 consecutive cases of kwashiorkor in Cape Town infection was the most important cause of death. Infection slowed the rate of recovery, and was present in a high proportion of the cases.

Treatment directed towards controlling infection and establishing a more normal intestinal flora resulted in a striking improvement in diarrhœa, more rapid recovery, and a fall in mortality. In this series mortality was 15%.

Better criteria of severity of kwashiorkor are needed. Muscle power, measured in a simple way, has been used as a criterion.

The average gain in weight in a large series of cases could be more widely used in comparing the efficacy of different forms of treatment. The complicating effects of infection and possibly disturbed intestinal flora should be controlled as far as possible before comparing one dietetic régime with another.

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TREATMENT OF RECURRENT STYES

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A STYE is a furuncle of the eyelash follicle, caused by *Staphylococcus aureus*. The sporadic stye appearing as an isolated incident is a self-limiting condition of minor importance; but recurrent styes present a different problem. The styes may be so severe and frequent that the patient is partially disabled, though in every other respect he may be healthy. This condition is often refractory to every form of treatment, the therapies being as diverse as the ætiological hypotheses. The potential danger is illustrated by the two patients who were admitted to St. Thomas's Hospital last year with cavernous-sinus thrombosis following a stye. One of these died.

The aim of this study was to employ a rational therapy for the treatment of recurrent styes. It was discovered that these patients are nasal carriers of staphylococci and seem to be more susceptible to the staphylococcus than others. An antibacterial ointment was used to suppress the staphylococci in the anterior nares. In a control series the inert base of the ointment alone was used. The identity of these ointments was known only to the pharmacist and not to the prescriber. The bacteriological results were not studied before the end of the investigation. Thus the assessment of the patients was without bias. This treatment by itself was effective in breaking the run of styes and the results were statistically significant.

Procedure

The subjects of the investigation were patients who presented with a stye having previously had at least one within the previous month. Many had a continuous succession without any break.

Cotton-wool swabs soaked in sterile broth were used to collect samples from each of the anterior nares and from the eyelid margins of both eyes at every attendance of the patient. Nutrient-agar plates containing phenolphthalein diphosphate were incubated for eighteen to twenty-four hours—the phosphatase-positive colonies turned pink on exposure to strong ammonia. *Staph. aureus* was identified if the subculture was colonially typical and was coagulase-positive (Barber and Kuper, 1951, Hare and Thomas 1956, Hare and Ridley 1958).

Treatment

Patients received treatment to the anterior nares alone and none locally to the eyelids. Alternate patients were treated with the antibiotic ointment and with the control. The antibacterial ointment used was a neomycin-gramicidin mixture, 'Graneodin'. Both these antibiotics are effective against the staphylococcus.

All patients were given a careful and simple explanation of the rationale of the treatment, until their cooperation had been obtained. This was followed by a demonstration of the method of application of the ointment. A small amount was to be placed into each vestibule of the nose with a matchstick and spread by inunction with the little finger. In each patient the initial application of the ointment was four times a day for ten days.

Bacteriological Findings

The nasal-carriage rate of *Staph. aureus* in patients with the sporadic stye (i.e., less than one year) was similar to that of the general population. Eighteen patients were examined; from eight of these (44%) *Staph. aureus* was isolated.

In clear contradistinction to this was the finding that in patients with recurrent styes a proportion greatly exceeding that in the general population carried *Staph. aureus* in the anterior nares. Thirty-six patients were examined; from thirty-four of these (94%) *Staph. aureus* was isolated on one or more occasions.

Results of Treatment

Bacteriological proof was obtained of the clearance of nasal *Staph. aureus* from eleven patients with recurrent styes, following treatment with graneodin ointment. All these had styes which varied in frequency from a new one every few days to one or more a month. In each patient the clearance of the nose was accompanied by the cessation of styes. In another patient remission of a run of styes was observed to coincide with the spontaneous loss of nasal staphylococci.

Six of these patients after treatment have been free from nasal *Staph. aureus* for more than three months (shown by bacteriological examination on two or more occasions), during which time not one of these patients has had a single stye. Some have been followed up for longer periods, and have remained free of styes, but no bacteriological check has been maintained.

Six comparable patients of the control series (who were examined on three or more occasions and found to be persistent nasal carriers) had between them an excess of twenty styes during the same period. These patients had undergone similar courses of treatment with the inert ointment.

An additional three patients who were treated with the active ointment had their run of styes broken and remained free for three or more months. However, no bacteriological proof of nasal clearance was obtained as they defaulted in their attendance.

Some patients were found to be predominantly carriers of staphylococci on the margins of the eyelids. This state was not convincingly influenced by the nasal treatment alone. Outstanding was one patient (who was swabbed on five occasions over a two-month period). He continued to grow an infinite number of staphylococci from the eyelid margins of both eyes, though always the nasal swabs were sterile; he was exceptional, being the only one out of sixty-five patients examined in whom this discrepancy was found. However, local treatment to the eyes themselves in such cases would be expected to clear the organisms from this site.

Discussion

In health *Staph. aureus* is isolated commonly from many areas of the skin.

It is more constantly found in the anterior nares (Miles 1941). Evidence derived from phage-typing indicates that it is from this site that the organism is most frequently disseminated (Miles et al. 1944, Williams, 1946, Moss et al. 1948), and now it is assumed generally that the anterior nares are the principal reservoir of the organism.

Gould and McKillop (1954), citing numerous sources, give these average estimations of the normal nasal-carrier rate: 85% in infants, 57% in children, 45% in adolescents and young adults, 50% in adults, and 65% among hospital staff. These figures are much higher among patients with superficial staphylococcal skin sepsis (Valentine and Hall-Smith 1952, Tulloch 1954, Gould and Cruickshank 1957). All these workers found that the phage type of the staphylococcus in the nose was identical to that in the lesion, notably if this was a chronic lesion on the face (e.g., sycosis barbæ). They showed that, whichever site had been primarily involved, it was imperative to sterilise the nares simultaneously for the treatment to

succeed, and that reinfection from a fresh source was rare. This view was endorsed by Roodyn (1954) in what appears to be the only published report of an investigation on styes. In this he found seventeen out of twenty-two patients with styes (both recurrent and sporadic) to be carriers of *Staph. aureus*, and in all the phage type of the organism in the nares and the lesion proved to be identical.

Duguid and Wallace (1948) and Hare and Thomas (1956) showed that the skin, handkerchief, clothing, and bedding are contaminated with nasal secretions containing the staphylococci, whence the organism constantly recolonises the individual. Non-nasal sites may also be important reservoirs (Hare and Ridley 1958). The fingers become readily contaminated; thus self-inoculation of the eyelids is an easy step.

Also from the present study it emerges that the staphylococcus can be carried persistently on one or both eyelid margins, usually in association with nasal staphylococci but occasionally alone.

Attempts to control superficial staphylococcal infection by suppression of the organisms in the anterior nares have been made by many workers using various agents. (Delafield et al. 1941, Burrows et al. 1945, Hobbs et al. 1947, Moss et al. 1948, Gould and Allen 1954, Tulloch 1954, Rountree et al. 1956, Gould and Cruickshank 1957, Gould 1957, Gillespie 1957).

The antibacterial ointment was chosen on this basis. The disadvantages of local application of antibiotics used systemically include the following: (1) that resistant strains of organisms may be induced and dispersed; and (2) that the carrier may become sensitised to the antibiotic, precluding systemic administration later. The disadvantage of the lesser-used topical antibiotics is that they are less potent for suppressing *Staph. aureus*, both at the time of application and afterwards. Thus in this series it was found, as did Gould (1957), that the nares of many of the carriers had been recolonised within four weeks. On balance, for this relatively benign condition the employment of the lesser-used antibiotics would seem to be indicated, and resistance to them as yet is rarely found (Elliot and Hall 1957). Their apparent failure in another series (Rountree et al. 1956), and probably in this one, was due largely to unconsciencious use by the patient, the organisms continuing to be sensitive to the antibiotics.

Conclusions

The great majority of patients with recurrent styes carry *Staph. aureus* in the anterior nares. Some patients carry the organism on the eyelid margins also.

Although treatment of the nares alone is generally sufficient, it is logical to treat the stye itself also to avoid transference of infection. Therefore, it is recommended that the most satisfactory treatment for recurrent styes involves simultaneous application of " non-systemic " antibiotics to both eyelids and to the anterior nares. This latter should be done four times a day for ten days, followed at two-weekly intervals by courses of seven days' treatment. This is frequent enough to avoid recolonisation of the nares. The best combination of antibiotics is a neomycin-bacitracin mixture (Rountree et al. 1956, Gillespie 1957). The same ointment is used for the eyes and the nose. Ideally as much as is practicable of the patients' clothing and bedding should be cleaned, to reduce environmental recontamination. This regime can be expected to break the run of styes.

Summary

Over 90% of patients with recurrent styes were found to carry *Staph. aureus* in the anterior nares. This is a far higher figure than that found among the general population and among those who have styes sporadically.

The run of styes was broken in patients by eliminating *Staph. aureus* from the anterior nares only, by applying an ointment containing neomycin and gramicidin (' Graneodin ').

It is recommended that recurrent styes should be treated by an antibacterial ointment, applied to both the nose and the eyes, and not to the eyes alone as is common practice.

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GASTRIC ULCER IN ASSOCIATION WITH HIATAL HERNIA

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Collier, Hurst, and Sheaf in 1929 reported two cases of gastric ulceration associated with hiatal hernia. In both the ulcer was on the lesser curvature in the " isthmus " of stomach between the hernia and the abdomen. Since that time gastric ulceration at the level of the diaphragm, in association with hiatal hernia, has become well recognised. The ulcers described by Collier et al. were large, chronic, and penetrating. Such ulcers are easy to recognise by radiography, but recognition at an earlier stage may be more difficult. A gastric ulcer may develop in a so-called gastric-lined œsophagus, or in the herniated portion of stomach. Such ulcers have been well described by Barrett (1950, 1954), and by Allison and Johnstone (1953). When the presence of a gastric ulcer is suspected, particular attention should be paid to the stomach at the level of the diaphragmatic hiatus both on preoperative radiographs and during the operation itself. At this site a non-penetrating ulcer may easily be overlooked unless specially sought.

The following case-records illustrate the features of this ulcer, and the type of hernia found in the first four cases is illustrated in fig. 1. This is described by Johnstone (1955) as a " sliding hernia resembling para-œsophageal type due to increased herniation of the greater curvature ".

Case-records

Case 1.—An obese woman of 51 had for some years suffered from heartburn. In October, 1957, she began to have severe pain under the left costal margin. The pain was most severe immediately after meals. It persisted and was but little relieved by alkalis. She became pale and listless. Hæmoglobin 41%. Occult blood was present in the stools. A barium swallow (fig. 2)

showed a hiatal hernia and a gastric ulcer at the level of the diaphragm. At œsophagoscopy, some œsophagitis was seen near the cardia with superficial linear erosions of the squamous mucous membrane, but no deep œsophageal ulceration. At operation (Feb. 18, 1958) an indurated area on the lesser curvature of the stomach was found, $1^1/_2$ in. from the cardia, and adjoining the anterior margin of the hiatus. Hæmorrhagic stippling appeared on its peritoneal surface when it was touched. The indurated area was not adherent. There was very little muscle tissue between the anterior border of the hiatus and the central tendon of the diaphragm. After reduction of the hernia, the patient experienced rapid relief from her pain. Tests for occult blood in the stools were negative a week later. The anæmia disappeared. A barium meal 14 days after operation showed no gastric ulcer.

Fig. 1—The type of hiatal hernia in cases 1–4.

Case 2.—An obese women of 69 had a history of postural heartburn for many years. For 2 years she had had severe burning pain in the epigastrium especially after meals. In April, 1957, she fainted and had hæmatemesis and melæna. She was tender under the right costal margin. Hb 49%. Occult blood present in the stools. A barium swallow (fig. 3) showed a hiatal hernia with a gastric ulcer at the hiatal level. At œsophagoscopy, little œsophagitis was apparent. At operation (May 14, 1957) there was found to be very little muscle tissue at the front of the hiatus. There was an indurated area on the lesser curvature 1½ in. from the cardia, lying against the anterior margin of the hiatus, but no adhesions at this point. The hernia was reduced. The patient had no further pain. Her anæmia rapidly disappeared. A barium meal 15 days later did not show a gastric ulcer. The patient has been symptom-free for a year.

Case 3.—An obese, dyspnœic woman of 60, with diabetes, was seen in 1954 because of severe epigastric pain which was persistent and not relieved by alkalis. Her gallbladder had been removed a year previously without relief. A subsequent X-ray showed a hiatal hernia but not a gastric ulcer. She continued to have epigastric pain and some heartburn, but because of her poor general condition was not operated upon. She was admitted on Oct. 13, 1956, with severe pain and tenderness in the left hypochondrium. For 3 months she had had repeated vomiting, occasionally of altered blood. Hb 44%. Œsophagoscopy showed moderate œsophagitis near the cardia but no ulceration of the œsophagus. At operation on the day of admission a non-adherent indurated area was felt on the lesser curvature 2 in. from the cardia and lying against the front of the hiatus. The hernia was reduced. A barium meal 17 days later did not show a gastric ulcer. The patient has had no pain for 18 months. The anæmia is cured.

Fig. 2—Barium swallow in case 1.

Case 4.—A woman of 70 had for many years complained of severe pain in the epigastrium and along the right costal margin. It occasionally radiated to her back. Her gallbladder had been removed without relief of symptoms. Hb 54%. A barium swallow showed a hiatal hernia but did not demonstrate a gastric ulcer. Œsophagoscopy showed no evidence of œsophageal ulceration. At operation on Oct. 23, 1957, the anterior border of the hiatus was felt as a firm, fibrous crescent. On the lesser curvature of the stomach, adjacent to the front of the hiatus and about 1½ in. from the cardia, there was an indurated area—more obvious on palpation than on inspection. Hæmorrhagic stippling appeared on its peritoneal surface when this was touched. There were no adhesions. The hernia was reduced. A barium meal 15 days later did not show a gastric ulcer. The patient has had continued relief from her pain.

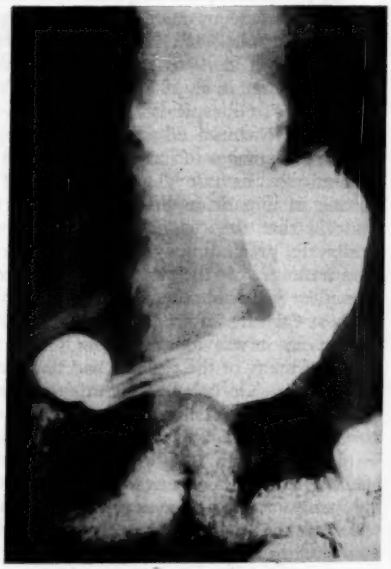

Fig. 3—Barium swallow in case 2.

Case 5.—A woman of 64 was admitted because of severe upper abdominal pain of a year's duration. 2 days after admission her pain increased, and radiography demonstrated gas under both domes of the diaphragm. The patient was known to have a hiatal hernia. No œsophageal ulcer was seen at œsophagoscopy. At operation (March 1, 1955) a para-œsophageal hiatal hernia was found: it contained stomach and greater omentum and there was some torsion of the stomach. At one point the greater curvature lay opposite the anterior margin of the hiatus, and here there was a perforated gastric ulcer of the greater curvature, adherent to (but not penetrating) the neck of the sac. The front of the hiatus felt hard, and consisted of compressed, indurated muscle tissue and firm central tendon. The hernia was reduced without difficulty and the perforation closed. The patient died suddenly of pulmonary embolism 14 days after operation. At necropsy, when the stomach was opened, the site of the ulcer could not be seen with the naked eye.

Discussion

Diagnosis.—After a long history of pain, indigestion, and heartburn, the patient develops more severe pain in the epigastrium or along either costal margin, sometimes going through to the back. The pain is inadequately relieved by alkalis and spontaneous remissions are infrequent. Hæmorrhage from the stomach may cause profound anæmia.

A gastric ulcer may be demonstrated by radiography, but its anterior position may make this difficult.

Fig. 4—Central aponeurosis of diaphragm, inferior aspect. (From *Quain's Elements of Anatomy*, after Blair.)

Operation and its effects.—The ulcer is commonly on the lesser curvature 1–2 in. from the cardia and the peritoneum over it is often not adherent at the neck of the hernia. During manipulation of the hernia, its contents are reduced into the abdomen. The gastric ulcer then lies some distance below the level of the hiatus. Its presence may easily be overlooked if attention is concentrated exclusively on repair of the hernia. The lesser curvature should be carefully palpated, because the ulcer is often discovered more readily by palpation than by inspection.

After reduction of the hernia the ulcer heals rapidly.

Anatomy of the œsophageal hiatus.—With a finger in the hiatus, one feels that, whereas its lateral and posterior margins are formed by a soft rolled edge of muscle, its anterior border is relatively sharp and firm. The central tendon of the diaphragm is in close proximity to the front of the hiatus and gives this margin its unyielding character. In the presence of a hiatal hernia, the muscle tissue at the front of the hiatus tends to be reduced, or compressed into a firm band at the back of the central tendon.

The most traumatic part of a hernial orifice is generally held to be its sharpest and firmest margin. An important cause of trauma to the hernial contents at the neck of a femoral hernia is the lacunar ligament originally described by Gimbernat. In hiatal hernia the firm anterior margin of the hiatus seems to play an equally traumatic part.

The portion of the central tendon lying immediately in front of the œsophageal hiatus is, moreover, its strongest part. As described by Blair (1923), the central zone of the diaphragm "is found to be occupied by four well marked diagonal bands radiating outwards from a central point of decussation like the bars of a St. Andrew's cross. This central point appears as a thick node of compressed tendinous strands situated in front of the œsophageal aperture" (fig. 4). There is therefore no possibility of enlargement of the hiatus in an anterior direction at the expense of the central tendon. To relate the anatomy of this hernial orifice to the more familiar external inguinal ring, the arrangement is reminiscent of the intercrural fibres which are described by Scarpa as "opposing further divergence of the tendinous pillars".

A portion of the lesser curvature about 1–2 in. from the cardia usually lies against the firm anterior margin of the hiatus, and it is at this point that the gastric ulcer commonly develops. In case 5, where the stomach had rolled upwards and undergone some degree of torsion, the greater curvature was at one point adjacent to the front of the hiatus; and here an ulcer had developed. It is suggested, therefore, that this type of gastric ulcer arises, not in relation to a particular part of the stomach, but on whatever part lies against the anterior margin of the hiatus.

The *cause of the ulcer* appears to be trauma. This is suggested by its exact localisation to that portion of the stomach lying against the firm anterior border of the hiatus, and by the fact that it heals and remains healed on reduction of the hernia.

These cases show that gastric resection is not necessary in the treatment of this type of ulcer. This opinion is based on experience with non-penetrating ulcers. If the ulcer is penetrating, resection of part of the stomach might be necessary (Barrett 1954); but, so long as the hernia can be satisfactorily reduced, surgery should presumably be as conservative as possible.

Summary

Five cases are described in which a gastric ulcer was associated with a hiatal hernia.

The ulcer developed where the stomach was in contact with the anterior margin of the œsophageal hiatus, and was apparently caused by trauma from this structure.

The presence of such an ulcer may easily be overlooked, even on radiography.

In these five cases the ulcer was cured without resection of the stomach. It healed as soon as the hernia was reduced.

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New Inventions

THIRD-STAGE BOWL

IN a report on maternal mortality issued by the Ministry of Health as a result of inquiries in England and Wales in 1952–54, the assessors expressed the opinion that in the postpartum hæmorrhage group 90% of the mothers should not have died. Deaths from postpartum hæmorrhage with retained placenta presented a higher proportion of avoidable factors than any other group. It was not always in the home that these deaths

took place; some took place in hospital, where attendants did not appreciate the dangers of slow, continuous hæmorrhage.[1]

Much of the blood lost after the delivery of the baby cannot be accurately measured. A loss of 20 oz. or more is usually regarded as a postpartum hæmorrhage.

A receptacle for collecting all blood lost after delivery was devised, in order to help to reduce the number of tragedies from this type of hæmorrhage. The essential feature of the bowl is that it has two lips, slightly different in shape, which will fit accurately into the perineum and inner posterior surface of the thighs with the patient lying in the dorsal position with the knees bent. The lips are also at different levels—one 3·1 in. and the other 2·7 in. from the base. These allow for the differences between primigravidæ and multiparæ, and thin and stout patients. After an extensive episiotomy, the bowl can be

1. Reports on Confidential Inquiries into Maternal Deaths in England and Wales, 1952–54. *Rep. publ. Hlth med. Subj., Lond.* 1957, no. 97.

tilted so that the catching edge is below the bleeding area. No handle is necessary—the lip not in use for receiving gives a suitable grip. The inside of the bowl is marked at levels 10, 15, and 20 oz.

This bowl has been in use in the labour wards of the Royal Maternity Hospital, Glasgow, and the sisters in charge state that all blood is easily collected and measured.

I am grateful to these sisters for their assistance when the prototype was being fashioned. The bowl is made by Messrs. Vicarey Davidson & Company, 162, Bath Street, Glasgow, to whom my thanks are due for their cooperation.

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Reviews of Books

Neoplastic Disease at Various Sites

Vol. 1. *Carcinoma of the Lung.* Editor: J. R. BIGNALL, M.D., M.R.C.P., assistant physician, Brompton Hospital; senior lecturer, Institute of Diseases of the Chest, Brompton Hospital, London. (General editor of series: D. W. SMITHERS, M.D., F.R.C.P., F.F.R.) Edinburgh and London: E. & S. Livingstone. 1958. Pp. 298. 55*s*.

THIS book, one of a series of monographs on neoplasms at individual sites, aims at giving a comprehensive yet detailed picture of lung cancer; and this aim has been brilliantly achieved. In the opening section general and regional trends of mortality from lung cancer in England and Wales are carefully analysed. In the next, Dr. Richard Doll discusses the causation of the disease, a subject to which he has so signally contributed. He reviews the evidence which has established the important role played by cigarette smoking, and considers how far industrial fumes, atmospheric pollution from chimneys and internal combustion engines, pulmonary scarring, respiratory infection, radioactivity, and heredity are implicated. After reading his estimate that in the absence of smoking the mortality from lung cancer in men would be reduced to about a fifth of the present figure, and that in women to about a half, some will be disappointed to find that no account is given of what preventive measures, if any, are being taken in this country and elsewhere.

In subsequent sections other authorities deal with pathology and laboratory diagnosis; the influence of such factors as site, cell type, sex, and age on the course of the disease; and the scope and results of different forms of treatment—surgery, radiotherapy, and chemotherapy. Only the less common clinical manifestations of lung cancer are discussed; descriptions of familiar forms of presentation, readily available elsewhere, have rightly been omitted. At the end of each section there is a summary and an extensive bibliography.

Reports on such matters as survival-rates and the incidence of different cell types are often misleading because of biased case selection; in this work the greatest care has been taken to put clinical phenomena in their proper perspective, and this aim has been successfully achieved because of the wide practical experience of the contributors, their highly critical approach, and the wealth of material on which they draw. The standard of presentation is uniformly high. This book is an unrivalled source of authentic information about lung cancer: anyone interested in the subject should get it.

Amphetamine Psychosis

P. H. CONNELL, M.D., D.P.M., consultant psychiatrist, Newcastle General Hospital. Maudsley Monographs no. 5. London: for the Institute of Psychiatry, Chapman & Hall. 1958. Pp. 133, 21*s*.

OBSERVATION of a methylamphetamine addict who developed "delusions of persecution and auditory and visual hallucinations indistinguishable from those occurring in paranoid schizophrenia", which disappeared after withdrawal of the drug, led Dr. Connell to collect the 42 cases of amphetamine psychosis on which this study is based. In 8 the psychosis developed after a single dose, in 4 while taking amphetamine and alcohol, and in 30 after regular doses for longer than a month. Because of severity of symptoms 39 had to be admitted to hospital, 26 to an observation ward. In nearly two-fifths of the cases the drug had been prescribed for tiredness, depression, or obesity. The range of dosage lay between 20 mg. dexamphetamine sulphate and 975 mg. amphetamine base. Many patients were alcoholics or addicted to other drugs as well—for instance, barbiturates. Apparently normal and well-adjusted individuals also reacted in this way, although two-thirds had a history of previous breakdown. Because of the absence of disorientation many were misdiagnosed as schizophrenics, and 4 had actually received a course of deep insulin on previous admissions for what in retrospect were clearly amphetamine-induced psychoses. Recovery within a week was usual, but relapse was frequent "owing to relapse to the addiction, which appears to be severe". Withdrawal symptoms were depression, often in excess of that for which the drug had been originally prescribed, and sleepiness.

Dr. Connell concludes that drugs of the amphetamine group are not harmless even in ordinary dosage in healthy people as has been generally believed, and that resultant psychosis is much commoner than would be expected from published reports. He provides a modification of the methyl-orange test for detecting amphetamine, dexamphetamine, and methylamphetamine in urine, which he suggests "be used in all cases of acute or chronic paranoid schizophrenia to prevent mistakes in diagnosis". This valuable study provides a timely caution against the light-hearted prescription of amphetamine and similar drugs, especially for such complaints as depression and fatigue.

Diagnostic Medical Parasitology

E. K. MARKELL, M. VOGE, assistant professors of infectious disease, department of infectious diseases, University of California School of Medicine, Los Angeles. Philadelphia and London: W. B. Saunders. Pp. 276. 49*s*.

THIS attractive book is a guide to clinical and laboratory diagnosis of protozoan and helminth diseases and, to a lesser extent, to the arthropods related to disease. It deals not only with parasites indigenous to the United States but also with others, such as the malarial parasites, which may be imported by travellers. The introductory chapter on parasitism and host relations takes the unusual view that parasitism is a form of symbiosis, in which one partner, the host, is injured by the other, the parasite; some readers may prefer to regard injury to the host as the feature which separates parasitism from symbiosis. Other chapters discuss methods of examining stools by means of wet films stained with iodine or other reagents, by concentrating protozoan cysts and helminth eggs or making permanent preparations and by cultivation of intestinal protozoa; the diagnostic features of intestinal protozoa and helminths; methods of examination of the blood for malarial parasites, trypanosomes, leishmanias, and microfilarial larvæ, and the features of these parasites. Elsewhere trichomonads, schistosoma, and the giant kidney worm, which all occur in the genito-urinary tract, are described, and later chapters discuss the tissue parasites (*toxoplasma pneumocystis*, tapeworms, trichinella, onchocerca, the guinea-worm, and the migratory helminth larvæ) and the arthropods. The last two chapters are devoted to biopsy, serological diagnostic methods, and other special techniques, including the use of fixatives and stains.

The short bibliography is confined to scientific papers cited in the text and might well have included standard textbooks on parasitology and the names of abstracting journals useful to the parasitologist. On the other hand, the excellent line drawings, coloured plates of the malarial parasites, and especially the photographs of helminths are outstanding. We have not seen before such lifelike photographs of the helminths. Most of these are by Mr. Zane Price and his colleagues in the department of visual aids of the University of California Medical School, and they are to be congratulated on their contribution to this valuable book.

THE LANCET

LONDON 4 OCTOBER 1958

ASME's First Conference

SINCE 1823 we and our contributors have rashly offered much advice about how to improve medical education; and no doubt it is fortunate that not all of it has been accepted. Nevertheless we cannot help regretting the low advice-action ratio that has been apparent in this country in recent years: a great deal has been said in support of reform in medical education, much of it wisely; rather little has been achieved. There has been an understandable reluctance to change or abandon familiar methods in favour of the new and untried; and in the matter of revising the curriculum the resistant ones were always able to fall back on the *Recommendations* of the General Medical Council, which, by the range and precision of their instructions, dissuaded British medical schools from introducing any of the changes they had been thinking about for so long. Since the *Recommendations* were relaxed, however, the opportunity thus afforded for experiment in medical education has been a challenge that many medical schools and teachers have been anxious to meet. And it was Experiment in Medical Education that the newly formed Association for the Study of Medical Education (ASME) [1] [2] chose as the subject of its very successful first conference [3] held last week in London at the Royal College of Physicians.

One of ASME's functions is to act as a forum for discussion, and if last week's deliberations provoked less public argument than might have been expected, that may be attributed to the inhibitions imposed by the unusual circumstances of a formal meeting of medical teachers actually discussing experiment. The calling of the conference was itself a notable experiment, and the drawing together of many distinguished medical teachers generated the atmosphere of enthusiasm and cooperation which is an essential preliminary to successful reform. The conference heard of change and progress in the medical schools of the United States and Sweden; and, though many of those present may have been familiar with what has been going on in these countries, not all had had the chance of hearing about it at first hand from those closely concerned, such as Prof. T. HALE HAM, of Western Reserve University in Cleveland, and Prof. B. REXED, of Uppsala. Such contact brought to life these educational experiments in a way that no written account could have done, and made possible an instructive contrast between the paths the reformers are following in the United States and Sweden. As Dr. JOHN BOWERS, dean of Wisconsin University Medical School, put it, the chief task of medical education is to marry in the student's mind scientific understanding with clinical art; and though the most effective method of doing so may vary from country to country, all medical schools can profit from a study of what others are attempting. In stimulating such a study by the exchange of information and by helping teachers to see what other schools are doing, the new Association can play a valuable part.

The objectives of medical education are not always very sharply in focus when reforms are being discussed, and in America and Sweden a definition of aims was regarded as a vital first step. A deliberate and conscious ranging of teaching methods alongside objectives was, Dr. JOHN ELLIS thought, one of the reasons for the success of Swedish medical education. The University Grants Committee, in their review [4] of the quinquennium 1952–57, have no doubt that the first duty of a university is to teach its students how to think; and in this capacity to think they envisage not only the power of ratiocination but more particularly " the ability to see the significance of facts and developments and their implications beyond the context in which they are first apprehended, and to exercise an independent judgment on the importance of facts and the quality of actions ". The success of this stimulation of the student's intellect depends not so much on the subjects he is taught as on how they are presented to him. The teacher, if he is to educate as well as instruct, must transmit enthusiasm as well as facts. The student must be brought to see that his first outlook on the university course, as a means to an end via examinations, was too narrow: he must begin to realise that intellectual pursuits are enjoyable for their own sake and " be given the sense of being in touch with creative work in which, if he does well, he may later be privileged to take part ". These qualities, once generated, can enable the student to go on learning for the rest of his life: if his university fails to instil them, it is unlikely that any later experience will make good the deficiency and enable him to develop his capacities to the full. At the ASME conference, Sir GEORGE PICKERING declared that medical education's chief failure was this inadequate training of the mind, and he returned to the attack on the examination system in this country as a stifler of thought with its largely descriptive questions that dulled rather than stimulated the intellect. For these and other defects Sir GEORGE blamed the attitude of mind of medical teachers; and it is to change that attitude of mind where necessary that ASME has embarked.

Examinations and what to do with them will certainly be one of the questions that will early engage ASME's attention; and the conference usefully indicated many other subjects for inquiry. How far can the methods of " operational research " described by Dr. NICOLAS MALLESON be useful in analysing the achievements of medical teaching, in pointing to improvements, and in

1. See *Lancet*, 1958, i, 1261.
2. The hon. secretary of ASME is Dr. J. R. Ellis, Royal College of Physicians, Pall Mall East, London, S.W.1.
3. The proceedings of the conference are to be the subject of a forthcoming issue of the *Journal of Medical Education*.
4. University Development, 1952–57. Cmnd. 534. H.M. Stationery Office. 1958. Pp. 92. 5s. 6d.

helping the student to a greater facility in learning? Should the student be exposed more deliberately to epidemiology and social medicine, as advocated by Dr. J. N. MORRIS? Can useful information be gained by analysing in detail particular features of our own educational structure which we judge to be valuable (such as the "firm" system in the clinical period) and identifying differences between the practice of various schools? Should the constitutional position of deans be fortified to give them more of the authority of American deans? Is research work a profitable stimulus to the undergraduate, or is it asking him to run before he can walk, as Prof. G. A. G. MITCHELL feared? Are British medical schools in need of a more personal and thorough method of assessing a student's progress? Above all, what means can be found to enable teachers to give more time to education and so remove a common hindrance to the introduction of a sounder curriculum —shortage of teachers' time? To gather the information and prompt the moves needed to answer these and many other questions, ASME is well placed; and we hope to see an increase in the number of its members, both individual and corporate, in many countries, and, in due course, a manifestation of its activities in the affairs of medical schools.

Surgery for Bronchiectasis

THE prestige of surgical treatment for bronchiectasis reached its zenith in the period immediately after the last war. Not only did it seem to offer the only hope of escape from a wretched, if not too protracted, progress to the grave, but recent spectacular advances in technique had greatly enlarged its scope: PILCHER,[1] for example, in 1946 reported the successful removal of damaged tissue from every lobe of a patient's lungs. Gradually, however, as the potentialities of chemotherapy became apparent the desirability of surgical intervention began to be reconsidered. Reappraisal of the role of surgery became necessary also as increasing use of bronchography brought to light more and more instances of bronchiectasis associated with only trifling symptoms or with no symptoms at all.[2 3] Since then, despite favourable reports of the results of resection,[4–7] surgical stock has been falling steadily,[8] and there is no indication that the bottom has yet been reached. It is difficult to get enough information to estimate the value of surgery, because it is uncertain how far the results of surgical and medical treatment in different series of cases can be compared, and controlled trials have proved impracticable. But much can be learnt from a well-documented study of the fate of patients treated by one method or the other, and a painstaking and extensive investigation by HELM and THOMPSON [9] of the results of surgery is therefore welcome.

They followed up 159 patients operated on by one surgeon between 1939 and 1952 for periods from $2^1/_2$ to 16 years (mean 6 years). 174 resections were performed on these patients. There were 3 (2%) deaths in the immediate postoperative period and 6 (3·5%) late deaths, giving a total mortality of 5·5%. It was found that of 118 adults in whom radical surgery was attempted 49 were cured, 29 much improved, 19 improved, 11 unchanged, and 2 worse; 8 had died. The corresponding findings in 29 children were 15 cured, 5 much improved, 7 improved, 1 unchanged, and none worse; 1 had died. Palliative resection was undertaken in 12 patients, and all except 2 benefited. The presence of generalised bronchitis adversely affected the results: of 32 patients so afflicted none was cured; but on the other hand only 2 deteriorated, and 24 improved to some extent. Bronchography was carried out on the side of resection in 100 patients 1–15 years (mean 5 years) after operation. Fresh bronchiectasis was observed in 13 of these cases, an increase of residual bronchiectasis in 13, and unchanged residual bronchiectasis in 10. Bronchography was also performed on the contralateral lung of 46 patients during the same period: it showed fresh bronchiectasis in 3 cases, an increase of residual bronchiectasis in 4, and unchanged residual bronchiectasis in 11. Deterioration was therefore noted in 26% of the isolateral bronchograms and in 15% of the contralateral. 25 of the 100 patients in whom bronchography was carried out on the operated side had generalised bronchitis, and 12 (48%) showed deterioration; whereas deterioration was noted in only 14 (19%) of the 75 patients without bronchitis.

Perhaps the chief interest of this investigation is the indication it gives of the circumstances in which resection is likely to effect a cure in bronchiectasis, for nowadays surgery is not likely often to be considered if it seems to offer less. HELM and THOMPSON's analysis makes it clear that the chief prerequisite of success is that the disease shall be localised, and that the affected tissue shall be completely excised. In "dry" bronchiectasis,[10] troublesome only on account of hæmoptysis, removal of the dilated bronchi can confidently be expected to give a good result, for disease is usually coterminous with the bronchiectasis. But when infection has been severe and long-continued, bronchi in neighbouring segments though not dilated may be diseased and are then apt to dilate postoperatively, especially if much adjacent lung has been removed. HELM and THOMPSON therefore emphasise that preoperative bronchograms should be carefully scrutinised for signs of bronchitis [11] in segments alongside those it is proposed to excise. They also point out that bronchography in children carried out under general anæsthesia may be misleading, and suggest that it is advisable to wait until local anæsthesia can be used.

Where it seems probable that surgery can offer a cure, the difficult problem arises of deciding whether it is worth accepting the risk entailed. Important considerations are the severity of symptoms after efficient

1. Pilcher, R. *Lancet*, 1946, *i*, 843.
2. McKim, A. *Amer. Rev. Tuberc.* 1952, **66**, 457.
3. Wynn-Williams, N. *Brit. med. J.* 1953, i, 1194.
4. Chesterman, J. T. *Brit. J. Surg.* 1951, **39**, 263.
5. Jones, R. S., Cole, F. H. *Sth med. J.* 1952, **45**, 101.
6. Lindskog, G. E., Hubbell, D. S. *Surg. Gynec. Obstet.* 1955, **100**, 643.
7. Ginsberg, R. L., Cooley, J. C., Olsen, A. M., Kirklin, J. W., Clagett, O. T. *ibid.* 1955, **101**, 99.
8. See *Lancet*, 1955, ii, 489.
9. Helm, W. H., Thompson, V. C. *Quart. J. Med.* 1958, **27**, 353.
10. Pinchin, A. J. S., Morlock, H. V. *Brit. med. J.* 1930, ii, 315.
11. Simon, G., Galbraith, H. J. B. *Lancet*, 1953, ii, 850.

medical treatment, the age of the patient, and the presence or absence of generalised bronchitis. It seems likely that nowadays any one physician will see only an occasional patient with symptoms bad enough to cause him to recommend surgery; deterioration with long-term conservative therapy seems to be uncommon.[2 3 12] The older the patient the less the appeal of radical measures, for the risk increases with loss of resilience.[13] In children, if symptoms are at all troublesome, it is hard to resist the prospects of final cure by operation, especially when bronchial dilatation is severe; without operation the prognosis as regards life is good, but exacerbations of infection may prove at best a nuisance and at worst a serious handicap. Moreover, when part of the lung is removed in childhood the remainder can fill the hemithorax by growing and not merely by stretching.[14 15] But in all cases of bronchiectasis in childhood lengthy observation is essential, and at the end of it the surgical harvest will probably be small.

Until more information is forthcoming about the long-term results of conservative therapy in different categories of bronchiectasis, it is clearly impossible to define the scope of surgery. But it seems safe to forecast that the need for surgery will continue to decline. Fewer operations for bronchiectasis are being performed today not merely because the place of surgery is being usurped by medical treatment, but because fewer cases of gross localised bronchiectasis are coming to light. In the past, two main sources of this type of disease in children were bronchial blockage from enlarged tuberculous glands, and pulmonary collapse during respiratory infections; these sources are of waning importance—the one because of the progressive eradication of tuberculosis, and the other because of more efficient treatment and improving social conditions. Possibly by the time it has been finally settled when best to employ resection for bronchiectasis there will be few opportunities to act on the knowledge.

Dealing With Disaster

IN the railway accident at Lewisham last December the immediate care of the casualties (as at Harrow five years earlier [16]) devolved on the ambulance service, police, fire-brigade, railway staff, mobile medical teams, St. John Ambulance Brigade, and volunteer doctors, who cooperated wholeheartedly and on the whole successfully, following a plan devised, at the instigation of the Ministry of Health,[17] after the Harrow accident. Subsequently committees were organised by Dr. J. S. S. FAIRLEY, senior administrative medical officer of the South East Metropolitan Regional Hospital Board, to study the Lewisham accident and to make suggestions for organisation and administration. These committees, which include representatives of the teaching hospitals in the region, have made considerable progress, notably in defining the duties of those called to the scene of large accidents.

In the London county area the ambulance service alerts the nearest designated hospital (i.e., hospital which by prearrangement shall if necessary provide a mobile medical team and accept a large influx of casualties), the police, and the Emergency Bed Service. The E.B.S. diverts normal emergencies from the hospitals in the area. A proposal, after the Lewisham accident, that each designated hospital should be responsible for a defined area has not been pursued, owing to lack of unanimity among the medical staffs of the designated hospitals in South-east London. The senior medical officer at the scene of the disaster is responsible for controlling and coordinating medical and first-aid resources and for formulating, in collaboration with the senior ambulance officer present, the casualty-evacuation plan. At the site of the accident the efforts of the various workers have to be integrated. The role of the police varies between different areas. In the London county area the police control traffic and crowds, protect property, and cooperate with other services; but the senior police officer on the spot does not act as incident officer controlling all services. In some other areas, on the other hand, the police take overall charge. In London the senior Fire Brigade officer present initiates the rescue plan; and the fire-control unit is to be the focal point in any future major accident.

The responsibilities of the senior medical officer of the mobile team can be grave; he must be able to speak with authority to police, fire officers, and ambulance officers, with whom he must decide on the need for alerting, through the police or by other means, mobile teams from other hospitals. It is unlikely that at first a consultant would be available, and a duty registrar of the designated hospital (possibly the take-in medical registrar) should act with the mobile team in the first instance. The mobile team should perhaps consist of a consultant, a registrar, and two casualty officers, supported by 2–4 dressers and 2–4 nurses. (The Ministry suggested that a team might comprise an experienced doctor and four trained nurses.[2]) The team which functioned at the Lewisham disaster were unanimous that they needed only morphine and simple shell dressings; but in addition a team should have at their disposal anæsthetics, dextran, and equipment for such occasional procedures as emergency amputations; all these should be kept in panniers in the hospital's dispensary. Infusions at the site of the accident are seldom essential: it is usually best to get the patient as soon as possible to hospital. When infusion on the spot is necessary, dextran is probably the agent of choice. Very rarely, for a trapped patient blood may be considered necessary; this should be sent by the hospital on demand. Reinforcement of the hospital supplies of blood for transfusion is a responsibility of the blood banks. (At the time of the Lewisham accident the South London Transfusion Centre at Sutton met all demands; and it is noteworthy that many donors reported spontaneously to Lewisham Hospital.) Arrangements have been made

12. Franklin, A. W. *Arch. Dis. Childh.* 1958, **33**, 19.
13. Gudbjerg, C. E. *Acta radiol., Stockh.* 1957, suppl. 143.
14. Miller, J. A. *J. thorac. Surg.* 1934, **3**, 246.
15. Bremer, J. L. *ibid.* 1939, **8**, 412.
16. See *Lancet*, 1952, ii, 1117.
17. H.M. (54) 51. See *ibid.* 1954, i, 1225.

whereby the regional blood banks can be reinforced, if need arises, from more distant banks.

At the site of the accident nurses, doctors, and others should wear distinctive uniforms; and they could usefully wear labels, such as "senior medical officer". There is also a clear need for a simple card that can be readily attached to the patient; and in the South East Metropolitan region mobile teams, ambulances, and the casualty departments of designated hospitals are supplied with these. Stretchers proved a difficulty at Lewisham, because many victims were brought in dead and their bodies could not be removed from the stretchers until additional mortuary space had been provided. It has been agreed with the London Ambulance Service that in a disaster it is unnecessary to follow the "one-for-one" rule; at most major hospitals the supply of stretchers (like that of trolleys) is insufficient. It is important that the stretchers have props that permit patients to lie on them on the floor.

The arrangements in the hospital receiving casualties cover the casualty department, the wards, and the theatres. Senior authority should rest with the medical superintendent in those hospitals which have one; otherwise it is best placed with the senior surgeon on duty, who himself should then be freed of immediate surgical work. There is a case for administering, equipping, and staffing the casualty department and mobile teams together. In addition to a consultant there would be four casualty officers and at least six nurses and six dressers: it would also be sensible to have the resident anæsthetist allocated to the casualty department at the time of a major accident. Few casualty departments in London can accommodate and care for more than 20 serious casualties at the same time. Arrangements must therefore be made for immediate expansion—generally into outpatients—when estimates of larger numbers are received. There must also be arrangements for the use of outpatient theatres, in addition to those in casualty, for the treatment of ambulatory patients. The designated hospital may have to evacuate, say, 15% of the occupied beds. When the hospital has received a prearranged maximum number of casualties—which may be as many as 100—further casualties must be diverted elsewhere. In the wards and theatre the surgical emergency plans of the hospital, which in general are covered by the take-in surgical and take-in orthopædic firms, could be expected to cope with the intake in the first few hours; but these firms may have to be reinforced. Similarly supplies of dressings, gowns, plaster, and so on may have to be augmented from outside sources. Communication may prove difficult, with all telephone lines to the hospital saturated by incoming inquiries. One solution is to have two ex-directory lines. The police plan a public relations office to deal with inquiries; and the B.B.C. could be asked to inform the public of its existence. In the Metropolitan area police will in future position radio-transmitter motorcars at the scene of the disaster and at the designated hospitals; and a similar system will be followed as far as possible in the rest of the region. The mortuary should if possible be in the hospital rather than in some outside buildings; but where there are many dead—at Lewisham there were 85—emergency mortuary space may be essential.

The possible contribution of the Armed Forces should not be overlooked; Services medical resources should be integrated in any plan—and indeed in most areas this has already been done. Perhaps Service representatives could be included in the committees organised by Dr. FAIRLEY, which are already doing most valuable work.

Annotations

BLANKETS AND INFECTION

HOSPITAL blankets have long been suspected of harbouring and spreading infection. They are, indeed, often teeming with bacteria—including, of course, *Staphylococcus aureus*. This is not surprising, because in most hospitals they are neither washed nor disinfected after use by each patient. There is, however, so far little evidence that dirty blankets are often responsible for hospital infection.

In this issue, Dr. Schwabacher and her colleagues at Watford report a trial of blanket disinfection. They describe a ward where *Staph. aureus* infection was not controlled until the woollen blankets were regularly washed and disinfected. They found, too, fewer bacteria in the dust of the wards when disinfected blankets were used. But after treatment the blankets quickly became recontaminated. Moreover, regular washing soon renders them unfit for use. Dr. Schwabacher therefore tried different types of blanket. Wool gave most contamination of dust in the wards. With 'Terylene' blankets contamination was 66%, and with cotton blankets only 13%, of that from wool. Staphylococci were greatly reduced in number but streptococci were not. Bacteriological investigations of this sort are not conclusive. Reduction of airborne contamination with streptococci, for example, often has little effect on the frequency of streptococcal disease. This may or may not be so for staphylococci, which may spread and infect by routes different from those taken by streptococci. Perhaps they do, because Dr. Schwabacher reports less cross-infection after routine blanket disinfection was begun, though she gives no precise figures.

In another article today, Mr. Pressley, of the Wool Textile Laboratories in Australia, reports investigations on the nature of dust in hospital wards. He found that cotton fibres were more numerous than wool and concludes that replacement of woollen blankets by those of other materials is unlikely to reduce cross-infection. These observations are difficult to reconcile with those of Dr. Schwabacher, who found more fluff in wards and more fibres on her culture-plates when woollen blankets were used. It would be interesting to know the composition of dust and fluff in the trial wards at Watford.

In yet another article this week, Dr. Bate and Dr. Ursula James report a series of intestinal infections in a children's hospital. Spread of *Salmonella typhimurium* was traced to dust, but the role of bedding was not investigated. Blankets are not the only items of bedding that may convey infection. Pillows and mattresses may do so. Terylene pillows, which are being tried at the London Hospital (see p. 743), may prove easier to sterilise than

down or feather pillows. There is still no method other than autoclaving for disinfecting mattresses; but these can be encased in plastic covers which are themselves easily disinfected, and which usually prevent infection reaching the mattress. Sheets raise no serious problem. Usually they are boiled in the laundry and are thus disinfected. Recently, lower temperatures have been used by the laundering industry for washing sheets; but these, too, seem to be satisfactory if they are not less than 60°C.[1 2]

There are many ways by which infection can spread in a hospital. The importance of each may differ according to the circumstances; but when infections recur over a long period, attention to the hygiene of bedding seems worth while.

REHABILITATION IN PSYCHIATRY

Dr. Walter E. Barton, who addressed a joint meeting of the Royal Society of Medicine and the Royal Medico-Psychological Association in London on Sept. 25, has a wide background, combining superintendency of the Massachusetts State Hospital with an associate professorship of psychiatry in Boston University. He described research in rehabilitation centred on the State hospital system, after remarking that rehabilitation was an attempt to utilise and develop a person's assets and possibilities, whereas treatment was an attack on his disability.

One study had covered four wards of psychotic patients. One male and one female ward—the experimental group—had received intensive rehabilitation including staff participation, educational, occupational, and recreational therapy, ward meetings and outings, and special social and psychological work. The other wards (of alternate cases) acted as controls. Progress and functional level were assessed after one year and three years. With acute patients it appeared that, according to the criteria of discharge and readmission, there were no significant differences between experimental and control groups except that rather more men and less women were discharged from the experimental group. With chronic patients the experimental group did significantly better as regards discharge, but showed marginal adjustment in society; again, women responded less than men. The study had an interesting stimulant effect on the control group but an adverse one on the staff, who, after early enthusiasm, resented the extra work entailed in the research. Rehabilitation, in some circumstances, appeared to act as a threat.

A second study, conducted by Dr. Ozzie G. Simmons and others, had been concerned with community aspects of rehabilitation since 1953. They described three stages in a patient's life after discharge: firstly, one of hesitation in which he doubts whether he can make it (possibly after a few days' initial confidence); secondly one of wider excursion in which he achieves some acceptable level of performance in relation to the family; and finally one of consolidation in which he experiences a progressively freer range of expression. Whether a patient could stay out of hospital depended on the tolerance of his environment. Mothers tolerated better than wives, and those patients stayed out longest whose families made few demands, did not expect them to earn wages, and accepted them in the status of children. Patients living apart from their families returned to hospital far more frequently. As was indicated in the discussion, the reverse has been found here by the Social Psychiatry Unit of the Medical Research Council [1]: the English family may be less tolerant, perhaps, but further comparative work is needed. Dr. Barton remarked that people's attitude is influenced by whether the goal of rehabilitation is simply discharge or, more ambitiously, a useful place in the community.

In a further investigation, at the Massachusetts Mental Health Centre, a very wide study was made of a rehabilitation scheme conceived as a link between three free agents—the patient, the hospital, and the community. One facet of this had been the use of vocational guidance; ex-patients finding work themselves did well, but those for whom it was found by an agency often failed to hold the job. A real work situation had been provided in hospital, and "work-tolerance" was increased to the point where a patient would manage an eight-hour day five days a week under normal conditions. Then he was given a course on job-finding. Employers willing to take ex-patients were contacted, but 40% of employers would only place discharged patients in unskilled jobs. The half-way house had been used experimentally with most encouraging results. About a third of those discharged were found to have very limited social contacts, and a further third continued to need fortnightly psychotherapy. In the discussion it was suggested, with regard to women, that success might be greater where the patient filled a housewifely role; perhaps the central kitchen will become a thing of the past.

All this new work is of the greatest importance and especially interesting to us here in view of the numerous experiments that are now taking place in British mental hospitals. Dr. Barton showed that things often thought to be unmeasurable can be measured, and that experiment must accompany reform. Aid must be sought from the social sciences, from psychology, and from statistics. It might be helpful to have a "mobile scientific unit" on circuit between the various investigations. The staffs of many mental hospitals are already doing valuable work; but wider contacts should reduce the sense of isolation under which some are labouring, and in any event internal change can often best be judged objectively by external observers. The M.R.C., perhaps with the help of a special committee of the Royal Medico-Psychological Association, might possibly provide such help.

THE CAUSE OF TROPICAL EOSINOPHILIA

WE lately remarked that the cause of tropical eosinophilia (pulmonary eosinophilia, eosinophilic lung) remained obscure.[2] In India, Gault and Webb [3] had found granulomatous foci, massive eosinophil infiltration, and five pieces of tissue suggestive of larvæ in the enlarged liver of a child with tropical eosinophilia. The most distinctive of these specimens was identified by Prof. J. J. C. Buckley as the anterior end of a nematode larva, but more complete identification was not possible. The syndrome has been attributed (among many other suggestions) to human filarial infection, but there are valid objections to this hypothesis.[4] In Singapore, Danaraj et al.[5] found *Wuchereria bancrofti* microfilariæ in 5·5% of 902 subjects, yet none presented the clinical picture of eosinophilic lung. The relative prevalence of filariasis was about the same among Chinese, Indians, and Malays—unlike tropical eosinophilia, which is virtually confined to

1. Crone, P. B. *Mon. Bull. Minist. Hlth Lab. Serv.* 1958, **17**, 167.
2. Jerram, P. *ibid.* p. 170.

1. Brown, G. W., Carstairs, G. M., Topping, G. *Lancet*, Sept. 27, 1958, p. 685.
2. *Lancet*, 1957, ii, 478; *ibid.* July 12, 1958, p. 84.
3. Gault, E. W., Webb, J. K. G. *ibid.* 1957, ii, 471.
4. Danaraj, T. J. *Quart. J. Med.* 1958, **27**, 243.
5. Danaraj, T. J., Schacher, J. F., Colless, D. H. *Med. J. Malaya*, 1958, **12**, 605.

Indians despite their numerical minority in Malaya. Danaraj[5] was careful to exclude patients with microfilaræmia when studying the effects of diethylcarbamazine in the treatment of eosinophilic lung. But because this antifilarial drug dramatically relieved the symptoms of tropical eosinophilia and because the complement-fixation test with *Dilofilaria immitis* antigen was strongly positive in all cases, Danaraj et al.[6] postulated an infection with filarial parasites of animal origin. Full development could not take place as man was not a suitable host: hence the negative blood-films.

Unexpected evidence supporting this hypothesis has now been described in a preliminary note by Buckley.[7] In an investigation of the possibility that Malayan animals act as reservoirs of human filariasis, a volunteer was inoculated in July, 1955, with *W. malayi* larvæ of monkey origin. Microfilariæ were not subsequently found in the blood; but in November, 1955, the volunteer developed a cough and increasing eosinophilia, which by December had reached 60% of a total white blood-cell count of 20,400 per c.mm. Only symptomatic treatment was taken; the cough continued for three months, and eosinophilia of 30–50% persisted throughout 1956. In May, 1957, *W. pahangi* of cat origin was inoculated; and ten weeks later similar symptoms recurred, eosinophils increasing to 75% in a total white blood-cell count of 40,500 per c.mm. The cough and eosinophilia were quickly relieved by a course of diethylcarbamazine. The filarial complement-fixation test became positive to a titre of 1 : 80 in the first and 1 : 640 in the second episode.

This evidence strongly supports the suggestion that animal filarial infection causes tropical eosinophilia; and no doubt lung biopsy at night—for that is when the cough becomes most troublesome—will shortly confirm the identity of the parasite. But will it solve the problem of why Indians are so much more prone to the illness than other Asian peoples?

MOBILE ELECTROENCEPHALOGRAM SERVICE

THE value of electroencephalography in neurological investigation has increased in the past decade; and it is now recognised as an integral part of a full neurological service. But the apparatus is costly, and the knowledge and experience required for its profitable use still tend to limit its availability. The majority of neurological centres in this country provide this service; and electroencephalography is also practised in mental hospitals. These arrangements probably satisfy most of the present demand; but it may be doubted however whether this is as great as it should be, for the adequate investigation of all cases of epilepsy includes an E.E.G. even though the evidence provided is sometimes negative. In the differential diagnosis of vasomotor syncope, and even in the investigation of apparently cardiological causes of loss of consciousness, it may also be of value. The early recognition of localised brain damage, whether from trauma, neoplasm, or vascular change, may be greatly expedited by it. Its value as a screening-test for the psychiatric disorders which may be due to a structural brain lesion is increasingly recognised. And in the investigation of episodic behaviour disorders, especially in the young, it has an important place. These are some of its routine clinical applications. In addition there is a zone of psychiatric and neurological work in which the instrument is a useful research tool. Judged by its potential applications this method of investigation should without doubt be more readily available.

This problem has presented itself in Michigan, where E.E.G. facilities were badly distributed in terms of population. In 1951 a mobile E.E.G. unit was organised; and this has proved a success.[1] The number of patients seen in the past seven years has increased from 95 to 190, though the mileage covered has remained much the same. Technical advances, and especially the emergence of efficient transistorised machines, have greatly increased the portability of these instruments, and the providence of a mobile E.E.G. service for outlying hospitals and clinics is no longer much of a transport problem. Such a development, with mobile teams based on a well-equipped E.E.G. centre, might prove more satisfactory and certainly more economical in technical and medical staff than the multiplication of small units at peripheral hospitals. A growing demand for E.E.G. services is already apparent. It is as well to have some plans to meet this efficiently and economically.

THE RIGHTS OF THE AGED

THE care of old people can be one of the most difficult duties of a community; and some of its problems have been sharply outlined by a recent case when a magistrates' court for the third time refused the appeal of a 90-year-old spinster for her freedom and extended by three months an order for her detention in hospital.[2] Her chief difficulty was apparently not shortage of money but of domestic help. She had sufficient means but had been living in a neglected home and had no-one to look after her. The authorities were clearly reluctant to deprive her of her liberty, but they felt that in hospital she was receiving care and attention she could not get at home. The medical officer of health said that it was difficult for anyone to help her, for she was "such an independent old lady".

Everyone was anxious to do the right thing, and for this particular old lady a further stay in hospital may well be the best solution. But obviously she is unhappy not to be living in her own home, and her appeal makes clear once again the difficulty of assessing the community's right to interfere with the aged citizen's liberty. How far should we respect their preference for independence, discomfort, and even dirt to incarceration in the most hygienic surroundings? Old people who are living alone may not be the easiest neighbours. They may be uncertain in temper, irregular in their habits, sketchy in their cleaning, resentful of help and advice. Shaky hands, shortsightedness, and forgetfulness may bring risk of fire. Sometimes it may prove impossible to leave them to their solitary and frail independence. But before asking them to relinquish it, we should be sure that they are causing others danger and real distress rather than merely inconvenience and a perhaps irrational feeling of guilt. Dr. Droller's article on p. 739 suggests that often much help can be provided by a suitably organised outpatient department.

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1. Rolfe, A. L., Derbyshire, A. J., Bohn, Z. S. *J. Amer. Med. Ass.* 1958, **167**, 1723.
2. *Birmingham Post*, Sept. 26, 1958.

THE INDEX and title-page to Vol. I, 1958, which was completed with THE LANCET of June 28, is to be issued next week. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Special Articles

A GERIATRIC OUTPATIENT DEPARTMENT

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THOUGH the number of patients attending special clinics for the elderly is slowly rising,[1] the need for such clinics is not yet generally accepted. They are not, as sometimes supposed, in competition with the conventional outpatient departments. Their purpose is to supervise old people discharged from hospital, to investigate those awaiting admission, to rehabilitate the physically handicapped, and to help in restoring the lonely and mentally deteriorated to social life. These last, in particular, are a vulnerable group for whom psychiatrists have little time. They do not fit into the conventional psychiatric "club", and besides emotional difficulties they usually have difficulty in walking.

STAFF AND PATIENTS

The geriatric outpatient clinic at St. James's Hospital, Leeds, which has some of the features of a "day hospital", was formed in 1952 from a follow-up clinic and has gradually expanded.

It is held twice weekly in rooms next to the remedial gymnasium. (This allows the superintendent physiotherapist "to sit in" on cases in which his advice or report is required.) Though somewhat cramped, it has three cubicles for examining patients. Occupational therapy and X-ray departments are within easy walking distance. Electrocardiography is done on the spot, and full laboratory service is available. The staff consists of a part-time sister (S.R.N.), an assistant nurse, a Red Cross nurse, and the unit secretary.

Our patients nearly all have to be brought by ambulance or ambulance car. Arrangements for attendance have therefore to be made well in advance. Patients receive warning cards informing them when to expect collection. Transport is provided by the local health-authority ambulance service. Lists of patients to be picked up in the coming week are sent to the central ambulance station each Saturday. These arrangements, requiring considerable administrative ingenuity, are made by the unit secretary.

Patients are referred to the clinic in several ways:—

(1) By the family doctor asking for advice or remedial treatment.
(2) By other departments.
(3) By the geriatrician, after domiciliary visiting, either to obviate admission altogether or for observation before admission.
(4) For treatment after discharge. This is particularly important for the elderly hemiplegic (Droller 1956, Droller and Thornely 1956).

407 patients were seen in 1957. 64% were 70 years old or over. There were more women than men (275 as against 124), no doubt because women live longer and because they more often develop skeletal lesions (Hobson and Pemberton 1955, Sheldon 1948). Of the 83 patients with such lesions only 10 were men.

The patients fell into the following four groups, each with somewhat different requirements.

The 139 patients with *diseases of the central nervous system* needed a good deal of constant physiotherapy to keep the hemiplegias in training. Patients with paralysis agitans or with multiple sclerosis needed more social help and supportive treatment.

The 83 patients with *skeletal diseases* needed physiotherapy, and steroid treatment with constant electrolyte control. Many intra-articular injections were given. The osteoporotics needed, besides hormone therapy and spinal appliances, instruction on how to feed themselves adequately, and where necessary the almoner arranged to get supplementary allowances for them from the National Assistance Board.

The 135 patients with *general medical conditions* correspond most closely to those seen at any medical outpatient department.

The 40 *psychiatric* patients received no psychotherapy. We found that those who could not be persuaded to join other patients in social activities improved in the friendly atmosphere of the occupational-therapy department.

TREATMENT

Many of our patients are socially handicapped and are unable to get about on their own. They have lost some of the social graces, and retraining helps to fit them to live among other people. This makes the work of the occupational-therapy department important, for it trains them in the activities of daily living.

46 patients attended the occupational-therapy department for the full day twice a week. Of these 20 were from the psychiatric group. These included the depressions, the presenile dementias, and 2 of the senile dementias. Their relatives feel that they can cope with them the rest of the week.

52 patients attended for two half-days a week. Gradually the practice grew of holding two sessions a day, one in occupational therapy and one in physiotherapy. At first patients brought their own lunches, but soon they found their way to the communal cafeteria with its self-service counter. Finally we were able to provide a midday meal (against payment) in a special room for patients who could not walk to the cafeteria. A voluntary worker from the Leeds council of social service attends at lunchtime to help with the meals. For many of our patients these meals are the highlight of the day.

For physiotherapy, we rely largely on Guthrie Smith exercises and the restoration of balance in the case of hemiplegics, with the use of walking exercises between parallel bars. As far as possible, patients are taken in classes. Electrotherapy is available but comparatively little used. The standard walking-aids are the Marjorie Warren tripod and walking-sticks and, where necessary, elbow crutches.

It has been our experience that, apart from remedial training, social activities as such help the patients to get on better with their relatives at home. We are able to break the monotony of their lives: the patient returns home full of new impressions, and the relatives can cope until the next clinic day. The relatives are reassured that their patients are adequately looked after and safe while they are away. Where relatives go out to work we have to guarantee regular attendance to prevent loss of working time. Some patients come into hospital while their relatives are away on holiday. Patients are encouraged to be independent, to be neatly dressed, and to do as much as possible for themselves. The sexes are mixed and rivalry in achievement is encouraged, both in the gymnasium and the occupational-therapy department. Indeed, lack of competition is, we think, one of the chief drawbacks of schemes for domiciliary physiotherapy such as that described by Adams et al. (1957).

All patients are seen, when they first come, by the consultant or his deputy. After that formal supervision varies from case to case, but the consultant does a regular round of the gymnasium on outpatient days. As so many of our patients are referred back to their own doctors, the number of medical interviews per patient per year is low—4·4. Questions of discharge, further treatment, social difficulties, pensions, re-housing and the like are discussed at meetings with the almoner and the city's welfare services, in which doctor, physiotherapist, and occupational therapist all take part.

1. It rose from 8988 in 1951 to 18,401 in 1955 (Ministry of Health 1957).

Our department offers physical rehabilitation to the hemiplegic, the arthritic, and other physically handicapped patients, as well as to the mildly confused, and it has been possible to mix the groups of confused patients and the physically handicapped patients, to the great benefit of the former. Our chief aim is to prepare patients for domestic tasks; they are started off on small chores, like winding wool or washing up, and go on to handicrafts and the workshop.

Our policy of discharging patients is conservative. If there is any chance of social breakdown, we prefer to keep them, perhaps reducing the number of sessions to one per week, or less, and at the same time introducing them either to a disabled persons' club or an old people's club. People who have made a reasonable recovery are referred back to their own doctor. A hemiplegic patient of advanced age needs constant encouragement. Even when he can make no further progress with physiotherapy we ask him to attend at longer intervals (3–6 months) for reassessment and further courses of treatment if necessary.

RESULTS

Of our 407 patients 125 have been able to return to the care of their own family doctor, 214 are continuing treatment at the clinic, 56 have been admitted to the geriatric unit of the hospital, and 12 have refused to attend or died in their own homes.

The number of discharges is not a reliable guide to response to treatment; for, where their home conditions are unfavourable, patients may continue to attend though their health has improved. But at the end of the year 162 patients had responded to treatment, and 148 were stationary, against 85 who were deteriorating.

From the medical point of view the scheme has justified itself by saving hospital beds. We found that some patients who asked to be admitted to hospital could be treated as outpatients, though for a smaller number adequate diagnosis in outpatients led to speedy admission. We visit and examine many patients in their homes, but some patients can, of course, be more satisfactorily examined at the hospital.

For former inpatients the geriatric outpatient department is equally important, because it enables many patients to be discharged earlier. Since 1952 the number remaining in hospital for more than a year has been nearly halved and the number who stay between six months and a year has been cut by a fifth. The reduction for the first group of over one year may be due to several causes (local-authority policy towards frail ambulant patients, for instance), but the reduction in the second group is almost entirely due to the earlier discharge of hemiplegics who return to outpatients for regular supervision.

Relatives need as much reassurance as the patients. We have found that relatives are glad to undertake the care of patients when outpatient treatment can be arranged. This is particularly true of psychiatric cases, so long as the patient remains socially acceptable to the neighbourhood. Disturbances of behaviour are more easily manageable if the patient can share for some part of the week in the life of a bigger community.

COST OF THE SCHEME

The cost of a geriatric outpatient department is not easy to assess. Accurate costing figures are not available. On the basis (Ministry of Health 1950) that 5 outpatient attendances equal the cost of 1 inpatient day (£2 in our hospital), our 11,829 attendances would cost £4721. The average cost of 5600 journeys between home and hospital, irrespective of the vehicle, was 10*s*., which adds £2800 to the cost, bringing the total to £7521. We held 93 sessions during the year, so that the total cost for each attendance was 12*s*. 6*d*. The average number of sessions attended per patient per year was 29. Adequate and reliable transport—a necessity for geriatric patients—is expensive. All who can do so use public transport, but most patients have to rely on the ambulance service. Without it the work would come to a standstill, as happened once when heavy snowfall made the roads of Leeds impassable.

Domiciliary Services

As the National Corporation for the Care of Old People (1957) has pointed out the cost of domiciliary services to the old varies from place to place and from category to category. For instance, to supply domiciliary services to old people who ought to be admitted to hospital may cost as much as hospital care, whereas reasonably healthy old people, able to live alone if given a certain amount of domestic help, may be kept at home for slightly less than it would cost to look after them in a local-authority hostel.

In our area in 1957 the cost of part III accommodation is slightly less than £5 per week per resident. The cost of a bed was £14 a week at St. James's Hospital, Leeds; £8 6*s*. 8*d*. at a long-stay annexe; and £7 9*s*. 11*d*. at a halfway house.

For an old person living alone we usually ask the home-help service of the local authority for six hours' help per week, which is almost always attainable and usually sufficient (Booth and Droller 1958). This costs £1 3*s*. 3*d*. a week, and two sessions at the geriatric clinic an estimated £1 5*s*.

The cost of keeping an old person at home thus ranges from £7 9*s*. a week to £3 15*s*., as the following budgets show:

	£ s. d.	£ s. d.
Old-age pension	2 10 3	2 10 0
Daily nursing service	2 2 7	
Home help (6 hours)	1 3 3	
Family doctor and drugs	8 2	
Geriatric outpatients twice a week	1 5 0	1 5 0
	7 9 0	3 15 0

The first patient costs only a little less than she would cost in a halfway house, but should she need more domestic help she would be as expensive to keep at home as in a long-stay hospital. The second patient is certainly cheaper to keep at home.

Personal services are now so expensive that as regards cost there is little to choose between treatment at home and in hospital, and the yardstick should be the efficiency of treatment. It may be worth while, as Shenfield (1957) has pointed out, to spend an additional £100 a year to keep an old person in his home rather than in a home or hospital bed. There is no doubt that many of our patients are happier at home than in the best local-authority hostel or hospital, particularly when there is a family (Townsend 1957). The Leeds unit aims at a compromise, combining short inpatient treatment with outpatient supervision, occupational day-centre activities, and physiotherapy, and our aim is to rehabilitate the patient and to reintegrate him into the community.

Even if the cost of domiciliary services plus outpatient treatment were to exceed the cost of inpatient treatment, we should still have to provide it, because the number of beds in our unit is constant but the demand for our help is always expanding.

I wish to thank the staff of the geriatric outpatient department; Miss G. Thornely, head of the occupational-therapy department; Mr. H. W. Poulton, superintendent therapist (St. James's Hospital

North); Miss C. M. Hargreaves, principal almoner; and Mr. H. Inman, deputy group secretary, St. James's Hospital.

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MENTAL HEALTH LEGISLATION IN SCOTLAND

THE recent Royal Commission on the Law relating to Mental Illness, by their terms of reference, only considered conditions in England and Wales. Legal procedure in Scotland differs in some ways from that of England, and a committee of the Scottish Health Services Council have been considering how far the Commission's recommendations can usefully serve Scottish practice. They concur [1] that the two main legislative changes proposed for England and Wales by the Royal Commission—the removal of the existing formalities for the admission and discharge of voluntary patients and of statutory distinctions between mental hospitals and general hospitals—should also be made in Scottish law.

The committee recommend in particular that the present written application for admission and the present three days' notice of intention to leave should be abandoned; that this recommendation should apply to all forms of mental disorder; and that statutory notification to the central authority should be abandoned. In recommending the removal of the existing distinctions between mental hospitals and general hospitals, they suggest that instead regional hospital boards should decide which hospitals and institutions may receive patients under compulsory powers and should then notify the General Board of Control. The committee propose that the word "mental" should be dropped from the names of hospitals and the official titles of boards of management, and the word "institution" in the case of mental defectives.

Though the committee consider that Scottish law and practice should be as similar as possible to law and practice in England, they do not think it justifiable to seek uniformity by sacrificing provisions which have worked well in Scotland.

Accordingly they recommend the retention of the present Scottish system whereby a sheriff's order must be obtained before a patient can be placed in compulsory care. They also recommend the retention of the General Board of Control for Scotland as a body whose main function would be to safeguard the interests of the patient, particularly the patient under compulsory care, but they suggest the board should be relieved of its duties as adviser to the Department of Health. The committee find it undesirable that the board should be asked to play simultaneously the parts of "referee" in matters affecting the patients' interests and of "centre forward" in the Secretary of State's mental health team. As patients may already appeal to the sheriff against continued detention, the committee think it unnecessary to adopt the system of mental health tribunals recommended for England and Wales. The committee also consider unnecessary the creation of a third category of mental disorder—the proposed "psychopathic" group. Those in it who would gain benefit from psychiatric treatment could, in their view, be included in one or other of the existing groups. To deal adequately with other people with psychopathic tendencies, who are often unsuited for ordinary institutional treatment, the committee believe that it would be necessary to set up additional special units, both under the National Health Service and the penal system.

The committee is now holding further meetings to consider the expansion of community care by local authorities.

1. Mental Health Legislation. H.M. Stationery Office. 1958. Pp. 15. 1s. The chairman of the committee is Mr. John Dunlop, C.A., and the medical members are Dr. J. T. Baldwin, Dr. P. K. McCowan, Prof. W. M. Millar, Dr. E. G. Oastler, and Dr. I. B. L. Weir.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

THE second provincial meeting of fellows and members of the College was held in Cardiff on Sept. 26 and 27, when Bristol and Cardiff acted jointly as hosts.

Eight medical films, made in Cardiff and Bristol, were shown. These included demonstrations of operations on the hand, of the removal of spinal tumours, and of sound recordings of alimentary and intestinal noises. There was also an impressive scientific exhibition, with forty sections depicting the work of the Bristol and Cardiff hospitals. Especially interesting among this array were demonstrations of the microsurgical techniques used for operations on the ear, and of the treatment of intracranial aneurysms by encasing them in a self-curing acrylic material applied in a semisolid state. The normal spine and its various pathological conditions were beautifully demonstrated by means of thin sections mounted on paper, using the Gough-Wentworth technique which was developed in Cardiff for studying lung diseases. More than 300 delegates viewed this exhibition, and there was a general feeling of regret that more time could not be devoted to it.

At the annual meeting of fellows and members, held under the chairmanship of Sir James Paterson Ross, the president, Sir Harry Platt made an appeal for financial assistance for the general funds of the College, and there were reports on its postgraduate educational activities, its research projects, and the reconstruction of the museum.

Sir Russell Brain was admitted to the honorary fellowship. In presenting him to the President, Prof. Lambert Rogers said that Sir Russell is the only living physician on whom this honour has been conferred. He also thought the people of Wales would be interested to know that a Prince of Wales (who later became King Edward VII) was made the first honorary fellow in 1900.

At the annual dinner the toast of The College was proposed by Sir Philip Morris, vice-chancellor of Bristol University. Responding, the President said he felt it was most appropriate that the meeting should be held in Cardiff during the year of the festival of Wales.

Public Health

Water Fluoridation

FROM A CORRESPONDENT

YOU may take fluoride to the people, but you still cannot make them drink it. The World Health Organisation expert committee on water fluoridation has published a level-headed technical report to encourage the practice; but Andover Corporation has been forced to a High Court settlement to stop doing so; and the East Worcestershire Waterworks Company is so uncertain whether it has legal powers to add fluorine that it has refused to do so when asked by three local authorities in the supply area. This ironical situation reminds us that scientific victories will be of little avail if the political battles are lost.

We have had our fill of reports for and against fluoridation. It would be ungenerous to deny that many of the writers have made valuable additions to knowledge, but to the ordinary reader there comes growing tedium and impatience with the repetition of mutual acknowledgments and the lists of fifty to a hundred references. Samuel Johnson once remarked that a man will turn over

half a library to make one book. With such arsenals of accumulated prejudice it seems most unlikely that the fanatics on one side will convince the fanatics on the other by any reasoned argument. Moreover it is high time that distinction should be drawn between the ingestion of fluorides and the fluoridation of the public drinking-water. The confusion between these is the cause of a lot of unnecessary strife.

The relator action in the High Court against Andover Corporation would have been fought not on the issue of whether the ingestion of fluorides was a good thing or a bad thing, but on whether the Corporation's practice of putting fluorides in the public drinking-water was ultra vires. No doubt some interesting arguments would have been put forward on both sides if the settlement of the action had not been precipitated by the political downfall of the pro-fluoridation members of Andover Borough Council. We may have to await protagonists with feet of firmer clay to test that particular issue. Meanwhile it would be a simple matter for Parliament to remove water undertakers from jeopardy by granting them statutory powers specifically to add fluorides or anything else to the public supplies, or even to compel them to do so. That is what the East Worcestershire Waterworks Company has decided to wait for. With the rolling of heads at Andover, and the unpredictable mass emotions stirred up by years of controversy, it seems most improbable that any Government would choose to invite political danger on the issue of whether people shall have holes in their teeth or not.

There is a strange contrast in policy between smallpox vaccination and fluoridation. It is not long since the central Government gave up forcing every private citizen towards vaccination: now it rests with the individual to decide. At no stage were the local authorities granted discretion to decree that all the people in their area should be vaccinated. The choice for fluoridation has not been offered to the individual in the same terms. He has little option but to submit to the majority opinion in his locality, and, as no neighbourhood is likely to express a unanimous opinion on anything, political strife is the inevitable result. The Government, always very sensitive to local-authority reaction, have been careful to refer to the current British fluoridation as demonstrations rather than experiments, and to emphasise that these are being done by resolution of the locally elected representatives of the people living in those areas. Such a line carries some suspicion of pre-judgment and a definite disregard for minority views. When the medical importance of smallpox and dental caries are compared, it is even more curious to see the extent of the paradox.

So, putting aside the scientific arguments, the legal uncertainties, and political expediency, the real problems about fluoridation seem to lie in the market-place. The common man has always impishly enjoyed the sight of experts in violent disagreement: when the technicalities of the issue are not clear to him he votes to maintain the status quo. He feels uneasy to seek the role of the experimental guineapig: he likes to cherish the myth that he has a free soul in a free man in a free country. He has gone to the stake and lands across the sea for that ideal before now. If he can choose cowpox lymph he can choose fluorine. He is uneasy at the choice of his public water-supply as the vehicle for making him better than he feels now. Water has some atavistic deep significance, a mystic quality, spa-like power. Civilisations have risen and fallen over water. Maybe those are some of the reasons why people are so touchy about it, why they resent its use for what they dislike as mass-medication, yet inconsistently clamour to have purified by their waterworks. Inconsistent and irrational it may be, but we have to recognise that it is deeply rooted in personal purification rites, in contemplation of the immaculate, in Genesis itself. Perhaps it is not so much fluoridation as the insensitive handling of a taboo that has aroused such strong emotions.

But to the general background must be added some factors that are characteristically British. Our public are mostly quite indifferent towards their dental caries: they have become accustomed to accept rotten teeth as part of our way of life. With the best will in the world, and even with the help of fluorine, they can never hope that Nature will fill their smiles with the regularity and dazzle of the poster hoardings. The toothpaste trade has set too high a standard for human frailty. What else could be the answer to this reminder of inferiority than to whip them all out as soon as may be, and choose something cosmetically better from the N.H.S.? Toothache banished, the fear of the dentist gone for ever: vie with the film stars by day, and discard them with other false vanities at night. That is certainly not what we preach as doctors and dentists, but that is a realistic picture of what faces us today.

So if we really want to tackle dental caries with fluorine or anything else, we might as well realise that blinding the public with science is a proven failure. It might work in unsophisticated countries, but it never works here. Fear, envy, and vanity offer much better chances. The responses to fear are unpredictable and might lead to even more premature dental clearance, apart from the ethics of such an approach. Envy seems to get results quite well. The poliomyelitis-immunisation campaign benefited greatly from the hard-to-get gambit, and by its advertisement as one of the more desirable features of transatlantic high standards of living. To a cinema-conditioned generation that appeal was irresistible. Waiting-lists piled up, rationing was introduced—and, after all, no-one yet has shown that the vaccine is as effective to do its own job as fluorine is for dental caries. The point lies in comparing the effectiveness of popularising preventive techniques. Envy wins hands down. Any sophisticated country contemplating fluoridation might well be advised to do so on such conventional political and commercial principles, and profit by our mistakes.

Vanity remains as the least despicable alternative to reason: it is a sin for which most people have a forgiving corner in their hearts. Fear and envy are unacceptable to our conscious thought, but in every reflecting surface we are daily reminded of our vanity. Proud though we may be of what our tailor or our dressmaker or our dentist have done for us, we cannot help wishing that the curves and the highlights were all our own. Could we not play more upon the public's vanity to show them that at least their teeth could stay all their own and be all that they could wish for? Reasoned argument has gone a long way to prove that fluorine can preserve the teeth, so let us see if we can offer it in some alternative way from putting it in the sacred drinking-water. After all, the public are quite accustomed to adding all sorts of drugs, chemicals, and panaceas into their tumblers and babies' bottles, so

surely they could be trusted to put in their own dose of fluorides if they feel like it. It is a battle for men's minds before their enamel.

Hospital Bedclothes

In hospitals articles made of wool—notably blankets—are gradually being discarded in an attempt to eliminate cross-infection. At the London Hospital bedclothes made of various different materials have been tested.

Blankets

Cotton blankets made of tufted towelling, cellular cotton, and turkish towelling, which can all be sterilised by boiling, have been tried.

The nursing staff find that tufted towelling blankets are the most suitable. These are cheap, do not deteriorate after many washings, and are surprisingly warm. Patients in wards without central heating, who previously had two woollen blankets, need only one tufted-towelling blanket, and they are usually relieved to have bedcovers of lighter weight. Cellular cotton blankets are less satisfactory because of their very loose weave, which makes them "catch" easily. Turkish towelling blankets are unduly heavy and thick, and they are much more expensive.

Cotton blankets are being introduced for routine use first in the operating-theatres, where the patients will also wear cotton theatre stockings. Woollen blankets will be banished next from the surgical wards, and later throughout the hospital.

Pillows

New types of pillows have also been tried, and 'Terylene' seems to provide a happy compromise between comfort and hygiene. Terylene pillows are as soft and light as down pillows, but they stand up to much harder wear; they are easier to sterilise, and will probably withstand boiling. Moreover they cost less than half the price of down pillows. Pillows filled with foam-rubber are firmer but they can easily be moulded, and are suitable for use underneath the softer terylene ones. They are less liable to harbour infective organisms than pillows stuffed with feathers or kapok, and they can be immersed in disinfectant.

'Jaconet' pillow covers are waterproof and boilable, but they are free from the cold, hard feel of plastic covers.

Drawsheets and Mattress Covers

'Playtex' drawsheets will soon replace the unpleasant, old-fashioned type of protective mackintosh for most cases. These are light in weight and flexible, and they cover the whole area of the mattress, so that they are less liable to crease under the patient, and they are cooler. From the nurses' viewpoint, they are much easier to handle and they can be sterilised by boiling. The need for routine fumigation of mattresses has been largely abolished by the use of close-fitting, waterproof covers made of plastic, which can be wiped over with disinfectant after each patient is discharged.

More Publicity for Health Departments

So long as things run smoothly and he does not feel the pinch too much, the average citizen is little interested in how the money he pays in rates and taxes is spent: he is content to leave the administration to Civil Servants and local-government officers. Thus in London, where the county council has a budget of many millions, only about one ratepayer in three goes to the trouble of voting at municipal elections. Admittedly the essence of democracy is that the voter has the right to do as he pleases and utterly neglect his own interests. Nevertheless many members of local authorities and most municipal officers would like their work to have more publicity and consequently (they suppose) better recognition.

In the United States it is common practice for commissioners of health not only to issue bulletins on their activities but also to appear on radio and television. The American doctor has neither the diffidence nor the inhibitions of his British colleagues and does not interpret his ethical responsibilities as narrowly as is done in this country. The best-known bulletin issued by a health department in a large city in America is probably the Monthly Health Bulletin issued by Dr. Huntington Williams, of Baltimore. His annual report also seems to be more widely distributed (3600 copies) than similar reports in England, and he was responsible for 528 film showings in 1955. A good example of the different approach to health education and publicity in the United States was Dr. Williams' action at the beginning of the anti-poliomyelitis vaccination campaign, when he highlighted the campaign by giving the first injection himself—with of course appropriate publicity. It is hard to imagine a British medical officer of health doing the same thing; but why not?

The immense influence of radio and television in public education is obvious, and in many directions both are fully exploited here; but whereas in the U.S.A. they are largely local, in this country they are primarily national and are less readily made to serve local purposes. Furthermore, the B.B.C. is relatively rigid and narrow in its insistence on adherence to certain formulæ, and in health as in other matters it seldom allows or encourages local broadcasts by representatives of local authorities. This is in striking contrast to Baltimore, where the city health department at the end of 1955 had given 852 radio broadcasts and 364 television appearances. It is interesting to recall that in pre-war days, when the city of Hull enjoyed a local broadcasting service, the medical officer of health, now Sir Allen Daley, made frequent broadcasts locally. Why is so little done in this way in the B.B.C. regions?

Most local authorities in this country now issue booklets, leaflets, brochures, and so forth, describing the services they offer their inhabitants; but in general these are strictly factual, and there is no human interest. The annual report of medical officers of health are apt to contain a lot of figures, and, with some honourable exceptions, they make dull reading for the public.

For the last two years the M.O.H. of Bristol, Dr. R. C. Wofinden, has been issuing, like his colleague in Baltimore, a monthly bulletin. This is by no means confined to recording the month-to-month activities of his department: it usually deals with some topic of current interest, presented in an attractive way. On the other hand it is not written for, or distributed to, the ordinary citizen, but only to the special groups of people who are in a position to interpret to the public the activities, the problems, and the views of the health department. Among these are all the local doctors (including those in the hospitals), the members of the health committee, the three local newspapers, the B.B.C. Western region, and (on request) members of overseas health departments. The clergy are not mentioned.

That these bulletins have been well received is scarcely surprising. They give notice—or warning—of local outbreaks of illness and epidemics; they outline the action the health department is taking, or proposing to take, on such matters as anti-poliomyelitis vaccination, the clean-air campaign, and the control of food infections; and they also deal with special problems—e.g., deaths by suicide, or the fat school-child. Arising out of some of the notes, four brief broadcasts have been given by members of the health department.

In England Now

A Running Commentary by Peripatetic Correspondents

THINGS have been different lately at our Fevers Group meeting. Instead of the friendly discussion, the amiable discourse, and the convivial cup of tea, there has been an atmosphere of nervousness, tension, and even fear. At one time all one needed to enjoy the meeting was a knowledge of the treatment of tuberculous meningitis, the place of serum in the treatment of scarlet fever, the theory of drug-resistance, and what was toxoplasmosis. But all that has changed since our new registrar came. At only his second attendance, after a most interesting paper on serum *v.* penicillin in the therapy of scarlatina, he gave us his thoughts on allergy and the psyche in disseminated lupus erythematosus. The silence which followed was, I am sure, composed more of sorrow than ignorance.

The next meeting was even worse. His paper on the place of sensitisation in the diffuse myelo-encephalopathies had us wondering where we last put the medical dictionary. When he was followed by the junior, who has his eye on the membership, detailing the nervous complications of sarcoidosis, complete with charts and line drawings, something akin to panic ran through the group. For once, the Chief's remarks on intrathecal streptomycin did not meet with the usual response.

And the rot has spread. Everyone is preparing a paper now. The library has become the scene of unparalleled activity, and almost every lunch-hour sees at least one harrowed figure frantically reading or feverishly scribbling. Even that is not all. A system of spying has been developed. The library withdrawal lists are being scanned, hints are dropped to discover the subjects of the next papers. Rumours abound on future presentations, quickly followed by hectic periods of reading, designed to compose questions which can be asked with that air of authority and familiarity. We even found our lady doctor in tears. After three weeks of reading on eosinophilic granuloma, she found the radiologist with the same case fully prepared and extensively documented. The Chief is beginning to look his age for the first time.

But there is hope. The Registrar was absent from the last meeting. Some say he is collecting his strength, others that he has joined the academic research group at the local teaching hospital. In the meantime we had a most enjoyable discussion on the treatment of tuberculous meningitis.

* * *

A few weeks ago, when I was visiting a hospital on behalf of a colleague who was on holiday, I recognised the registrar (a Commonwealth graduate) as one of my students on the last internal-medicine course and a prospective M.R.C.P. He took me round with great efficiency, and when we reached the last bed he said: "This patient was admitted this morning; the blood has not yet been examined, but I have diagnosed pernicious anæmia." I looked at the occupant of the bed; he was a deathly pale young miner, aged 29, with a hæmoglobin which could not have exceeded 25%. The spleen was large and soft. After we left the ward I discoursed on acute leukæmia and its tragic prognosis. During this time the house-physician had stained a blood-film which presented the textbook appearances of pernicious anæmia. Further investigation and the response to treatment have established the registrar's diagnosis.

Yesterday at my last visit I offered my congratulations on his clinical acumen and my best wishes for the membership. Then, aware of my responsibilities as an examiner, I added, "But, please, never again make a clinical diagnosis of pernicious anæmia in a man of 29." "No, sir, of course I will not," was the polite reply. As we shook hands his dark eyes betrayed bewilderment about the strange ways of fellows of the Royal College of Physicians.

* * *

It is our proud boast that, though tears are commonplace, screams not unusual, and hysterics exceptional, we have yet to lose a patient. Our record, however, almost ended last Friday. Little Jennifer—nervous, uncertain, and a bit frightened—was led into the surgery. On either side, each holding a hand, was her anxious trembling mother and her large protecting father who, notwithstanding the television programmes, tended to glare at us, the white coats, and the instruments in awful array.

The situation was explained as simply as possible. The necessity, the ultimate good, the relative lack of pain, and the almost negligible discomfort. Mother, staring wide-eyed at the bottles and syringes, said nothing; Father, grim and tight-lipped, nodded his consent. Reluctantly he surrendered Jennifer to the nurse while Mother, tightly holding a hand, tearfully told her to be brave.

The area was swabbed, dried, and swabbed again; the penetrating smell of surgical spirit filled the room. The syringe was filled and the nurses took up their positions. Jennifer, her eyes tightly closed, was slowly approached. A few soothing words were spoken and the needle descended.

The awful crash which followed petrified the medical staff more than it did little Jennifer. There lay Father on the floor, pale and unconscious, blood running freely from a nasty gash in the temple. For a moment confusion reigned. Jennifer cried, her mother screamed, and the nurses rendered first-aid. Order came slowly, but eventually Father was carried out to the waiting-room, moaning feebly, while Jennifer and her mother were reassured. Luckily the trolley from casualty did not take long in coming.

All ended well. Father's cut was cleaned and stitched, and the X-ray showed no fracture. Jennifer's Mantoux test turned out to be negative, and she will get her B.C.G. in a few days.

* * *

According to a recent advertisement in *The Lancet* (Sept. 20, p. 45) the Elmore medical research studentship of the University of Cambridge "is open to male graduates of any university in any country who were born at any place in the British Empire or Commonwealth other than in Scotland". Shades of Bannockburn, or was it Flodden?

* * *

Up here in the Welsh hills I was struck by the resemblance between farming and the health service. The farmer is the general practitioner and he has the help of ancillary services such as the ploughing experts with special equipment who help him to reclaim difficult hillside land from the relentless grip of the bracken. Consultant service is provided by the vet. who says he never goes to bed before 11 P.M. because of emergency calls, and then may be out at 2 A.M. to help with a difficult labour and even do a cæsar. An example of group practice is provided by the farmer who has a hay-baler and lends it to his neighbours, often working till late at night in good weather. But the service the G.P. farmer values most is one that is never likely to have many practitioners in the N.H.S.; it is that provided by the A.I. men, no less than four of whom are based on the local market town and give a 7-day-a-week service. A field with a bull in it is now a negligible danger for the nervous townsman on his rural walks.

But there is still plenty left for the G.P. farmer to do besides his ordinary day-to-day chores. With no more concern than a pathologist doing a blood-count he implants œstrogen pellets into the ears of lambs destined for the table, so as to produce a plump lean animal to suit the demand of the housewife; and with a special applicator he pops a 5 g. sulpha tablet down the throat of scouring calves, and discusses learnedly whether they should, like human babies and lambs, have "on demand" feeding. Small wonder then that he will sacrifice even a good harvesting day for a visit to the local agriculture show when modern science has so many important aids to offer.

* * *

News from holidays.—While the sun was shining yesterday I stung myself on a wasp because I had my leg down with short trousers on and the wasp craled underneath my leg and stung me. I have just seen a dragon-fly while I am sitting in sun having a game of Hostipal and Clare is been a bit naughty and rushing a round when she should not be while Janet who is maitren is off duty. As-well today it sunny but it mite rain.

Letters to the Editor

PREREGISTRATION POSTS

SIR,—Many of us in the peripheral hospitals are getting more and more concerned with the difficulty in appointing resident staff at house-officer and registrar levels.

Graduates of British universities tend to go to their own teaching hospitals for their preregistration appointments, leaving few for the non-teaching hospitals. However, it has come to our notice that many posts selfishly classed as preregistration posts in surgery at the teaching hospitals in all parts of the country are not strictly surgical posts as intended by the Goodenough report on medical education. Neurosurgical, E.N.T., anæsthetic posts with a few casualty sessions, and orthopædic posts are designated as preregistration jobs in surgery which we feel is against the principle of the Goodenough report, although perhaps not technically disagreeing with it. Similarly medical posts exclusively in hæmatology, rheumatology, and neurology fail to give the general experience envisaged by the report.

As 80% of graduates will ultimately settle in general practice surely the everyday medicine of the peripheral hospital is the ideal place for experience and not the hothouse atmosphere of the teaching hospital. As students they have already seen these selected cases.

If this type of special post were not designated as a preregistration job, many more graduates would be released for peripheral hospitals to carry out straightforward surgical jobs and so ease our difficulties in staffing. The teaching hospitals could designate these posts as senior house-officer. It is unlikely that there would be any difficulty in filling them and it would give many of the overseas graduates an opportunity to have an appointment at the teaching hospitals—surely a good advertisement and investment for us as a country in the Commonwealth.

RONALD SAVIDGE
B. WOLMAN
D. M. DAVIES.

Bury General Hospital,
Bury, Lancashire.

CONTROL OF THE COMMON COLD

SIR,—Much interest will be aroused by Dr. Morrison Ritchie's latest observations (Sept. 27) confirming the result of his earlier controlled experiments, that full development of a cold can often be prevented by administration of an " appropriate " antibiotic on the first day of symptoms. His method of applying a " tailored " antibiotic to previously measured cases—i.e., to patients whose nasopharyngeal flora have been tested within the previous 12 months for drug sensitivities—may have wide potential uses in industrial medicine but surely meagre application to the general population, who, moreover, do not usually report at the beginning of a cold. Perhaps some way must be found of restricting the use of his method, since he apparently gives the antibiotic in some cases at least over a period of " a few days ", and since, in his own words, the continued prophylactic use of systemic antibiotics may lead to the production of resistant bacteria and is therefore to be condemned. He recognises, however, that in an " emergency " their administration is open to no such objection.

Last spring, after reading Dr. Ritchie's first article on the subject, and within a few hours of onset of an undoubted cold I took a few capsules of the broad-spectrum antibiotics, chloramphenicol and oxytetracycline, over a period of 24 hours, and was pleasantly surprised to find that my cold did not progress beyond the stage of *watery* nasal secretion, and dried up in 24–36 hours. This, of course, might have been the kind of cold which would not have progressed beyond the prodromal stage in any case—a condition which, according to Ritchie's data, may occur in almost 50% of untreated persons reporting symptoms of a cold. However, a recent personal experience was more striking. I was one of a party of four who went on holiday with a group of some twenty people to a hotel in northern Portugal. On the third day the weather turned stormy and a lady in the group was going about with obtrusive symptoms of a cold in the head. At successive intervals of 3 days thereafter one of my party, commencing with myself, developed the typical symptoms—sneezing, nasal obstruction, and profuse watery discharge. Each of us was treated with chloramphenicol 500 mg. for 3 doses about 6-hourly followed by one of the tetracyclines (250 mg.) for 3 doses 4-hourly—a total of 9 capsules over a period of 24 hours. The treatment was commenced 5, 5, 9, and 10 hours respectively after the onset of symptoms. The result in all 4 cases was the same: perfect recovery within 36 hours without the appearance of any mucopurulent secretion. Meanwhile at least four other persons in the larger group had developed full colds (without treatment) and went about feeling miserable and with red stuffed-up noses for a week or longer.

It would seem worth while to try out this method on selected cases; it differs in detail from Ritchie's. I suggest chloramphenicol for the first 12 hours because of its known potency and wide range of action, and to follow on with a tetracycline in smaller dosage for the next 12 hours. This small dosage of each antibiotic must surely carry very little risk to the individual, and to the community only if practised very widely—which is unlikely since few patients report their symptoms within 12 hours of onset. The cost of these drugs is not negligible (approximating £1) but there is much to offset against this. There must be many circumstances in which the tentative and judicious use of such a method is justified.

Leatherhead. H. STANLEY BANKS.

EARLIER DETECTION OF LUNG CANCER

SIR,—With over 17,000 lung-cancer deaths annually in this country alone, we urgently need a method for detecting cases early enough to allow more cures than we can get at present. *Serial routine* radiography for this purpose is still unassessed and its theoretical potentialities have not been tested in practice. Nevertheless, I think it is unlikely that, even when used in an adequate scheme,[1] the beautiful 70 and 100 mm. photofluorographs that may be obtained with the latest ' Odelca ' cameras, will entirely suffice for our purpose of earlier diagnosis.

The single postero-anterior (P.A.) photofluorograph has the limitations of being taken from a single angle. This is probably adequate for the peripheral lung fields but not for the hilar and perihilar areas—those difficult regions of superimposed shadows where it is difficult to see the trees for the wood. Nor will the addition of a lateral view disentangle all the overlapping shadows. I suggest that what we need, in addition to the P.A. photofluorogram, is a multi-angle, preferably " live " (i.e., screen) view of the hilar and perihilar areas.

My impression is that, in the 5 in. Philips image intensifier, we have perhaps just what we need to allow us to visualise the separate components of the hilar agglomeration using the screening binoculars, while very slightly rotating the examinee as one makes the inspection. Because the image intensifier is capable of brightening the screen image up to a thousand times,

1. Nash, F. A. *Excerpta Med. Aust.* 1958, 3rd International Congress of Photofluorography; p. 9.

we can use minute milliamperages, and a thirty-second examination of the hilar areas can be made with 0·1r, an amount that we can easily "knock off" the photofluorographic examination by using the new faster films, &c., which are about to be released—thus allowing two examinations for less radiation that is currently received at one.

Briefly then I suggest that, for earlier detection of lung cancer, we *may* have a new hope in the synergistic use of separate diagnostic techniques—e.g., photofluorography and "live" multi-angle inspection by image intensifier of the hilar and perihilar areas. At the six-monthly routine examinations of males over 50 years of age that will be necessary in any effective lung cancer control scheme, the results of interrogation would be also available. For example, some examinees will tell of the presence of unusual cough for which they have failed to consult their doctors. Such answers would provide another factor in the synergistically obtained measure of degree of suspicion on which the need for further investigation may be decided. The value, if any, of these proposals can only be assessed in practice.

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London, S.W.6. F. A. NASH.

PROTEIN MALNUTRITION AND THE PANCREAS

SIR,—While protein malnutrition, whether primary or secondary, plays an undoubted and significant role in initiating pancreatic lesions, it seems difficult to relate the most interesting case-reports by Dr. Leitner (Sept. 6) to the extensive discussion which follows these reports. If I understand the intention of his communication, it is suggested that in these two patients a typical syndrome of secondary protein malnutrition developed some years after pancreaticoduodenectomy, leading to pancreatic damage which was reversible in case 2, but which became irreversible in case 1.

In his case 1, the head of the pancreas was resected for obstruction due to chronic pancreatitis, and steatorrhœa was found to be present some two years later. In a patient with established chronic pancreatitis it seems unreasonable to postulate that protein malabsorption had led to further acinar atrophy and fibrous tissue replacement of the pancreas, and there can be no possible comparison between this type of condition and kwashiorkor. In his case 2, severe steatorrhœa followed resection of the head of the pancreas, and while protein malabsorption as indicated by œdema and low serum-albumin levels was a marked feature, there is no reason to believe that this secondary protein malnutrition had led to fibrosis in the pancreas, nor in fact is there any reason to postulate such damage to account for the steatorrhœa.

Protein malabsorption is a well-established feature of both pancreatic and idiopathic steatorrhœas, but it is unusual for *severe* impairment of protein absorption to occur in either of these conditions; Adlersberg et al.[1] noted serum-albumin levels of less than 3·5 g. per 100 ml. in 52% of their patients with idiopathic steatorrhœa, 24% of this group presenting with œdema, while Forshaw [2] and Wahlund and Westad [3] have described patients with even more severe protein malabsorption. Secondary protein malnutrition may certainly lead to changes in the pancreas but in the two patients described by Dr. Leitner, while their degree of protein malabsorption is noteworthy, there is pre-existing proven chronic pancreatitis in case 1, and no evidence of pancreatic lesions induced by protein deficiency in case 2.

The use of the term "secondary kwashiorkor" for this type of problem (albeit in parenthesis) should be discouraged for there is little in the ætiological backgrounds of these two conditions to make them comparable, and the clinical resemblance is rarely marked. The terms "kwashiorkor syndrome" or "adult kwashiorkor" have previously been used to describe a variety of nutritional states, and Krikler and Schrire [4] have applied "adult kwashiorkor" to a patient with a blind-loop syndrome and secondary hair changes. The remaining references made by Dr. Leitner to the protein malnutrition syndrome [5–7] have a far greater claim to the use of the term and no matter what the clinical appearance, it seems unsupportable to extend its usage to postoperative conditions not primarily associated with a dietary deficiency of protein. It should be emphasised in passing that the term "kwashiorkor" does not refer to the red colour of the hair or skin, and the term is now accepted as meaning "the deposed", implying the weaning of the child on the arrival of the next baby. If "adult kwashiorkor" is to be used at all, it should be limited to those patients with a history of protein malnutrition and the characteristic pathological and biochemical changes seen in children with kwashiorkor.

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A USEFUL ACCESSORY SUTURE

SIR,—I thought it might interest Professor McFarland [8] to know that the "dodge" he has used for many years has been reported [9] by my former professor of surgery, Dr. Daniel LeRay Borden, of Washington, D.C.

George Washington University
School of Medicine,
Washington, D.C. ALEC HORWITZ.

MINAMATA DISEASE

SIR,—I was interested by Dr. McAlpine and Dr. Araki's paper (Sept. 20) describing an outbreak in Japan of an unusual neurological disorder. They think that the disease was probably caused by eating fish contaminated by the effluent from a fertiliser factory. I wonder if they have also considered the further possibility that it might have been due to some natural poison in the fish? Certainly fish can be poisonous, especially if eaten raw as is seemingly the common practice at Minamata.

Foxes fed raw carp develop a paralysis which is due to an antivitamin in the fish, antagonising thiamine.[10] Cooking the carp destroys the antivitamin.

The human disorder known as Haff disease in Sweden has been thought to be due to eating such fish as pike, perch, bream, roach, eel, and burbot.[11] At certain times, some natural component in the food of these fish seems to make them poisonous. It would be interesting to know what species of fish are commonly eaten at Minamata, and whether there had been any changes in the plankton on which they feed.

But if the factory effluent was really to blame, we must hope that by now something has been done to control it, and that the fishermen are back once more in Minamata Bay from which they were banned in November, 1956. Fish is the principal source of animal protein for millions of Japanese children.

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TONSILLECTOMY AND POLIOMYELITIS VACCINE

SIR,—A boy aged 6 years had his tonsils removed three weeks ago. While the boy was in hospital for tonsillectomy his father became ill at home with headache, neck stiffness, and backache. This illness cleared up after a few days, but a fortnight after returning home the boy developed bulbar poliomyelitis. The father's illness must have been non-paralytic poliomyelitis, but tonsillectomy made sure the son's attack was bulbar.

The relationship between tonsillectomy and bulbar poliomyelitis is accepted. Poliomyelitis vaccine almost certainly gives some protection against the disease. Is there any justification for carrying out tonsillectomy in children, or adults, who have not been inoculated against poliomyelitis? It should very seldom be difficult to postpone the operation till two injections of vaccine have been given to the uninoculated, or a booster dose to those already inoculated.

Fazakerley Hospital, Liverpool. A. B. CHRISTIE.

THAT DAMNED WORD HEALTH

SIR,—I suspect Dr. Gordon had his tongue in his cheek when he referred, in his interesting and valuable paper of Sept. 20, to his colleagues in the Public Health and School Health Services.

Does he want to change the term "public health" to "public medicine"? They do not mean the same thing, do they? And certainly I do not know that my colleagues (and his) in the School Health Service wish to change the title of their service, as he suggests. It is *not* a school disease service; that is a concept long since outmoded, because conditions have changed.

He is right to point out the necessary antithesis of health and disease, and right to point out, by inference, that doctors are by education and experience the ones best fitted to be responsible for the organisation of services whose primary purpose is the maintenance and improvement of health.

Whether public-health and school-health doctors will ever get a fair deal in their salary—ah! that's another question.

Health Department, Exeter. E. D. IRVINE
President, School Health Group, Society of Medical Officers of Health.

PSYCHOLOGY OF LABORATORY ANIMALS

SIR,—I was more than surprised to read in your issue of Sept. 20 (p. 632), in the course of a report on the current activities of UFAW, the following sentences:

"A second hope is a reduction in the number of animals needed for a given degree of precision . . . by detection of specific factors which effect variance. On the last point, UFAW is sponsoring a research directed again by Dr. Chance in Birmingham. (The last-mentioned research, incidentally, inaugurates a long overdue study of the psychology of laboratory animals.)"

Far from being inaugural, any research of this kind must come as the next step in the now considerable volume of work in this field which has been undertaken during the present century. For example, N. L. Munn in his *Handbook of Psychological Researches on the Rat*, which was published in 1950, gave a bibliography of over 2000 papers devoted to studies on the psychology of the laboratory rat alone. Since 1950 there has been much additional work done in many parts of the world. It is probably true to say that in many respects we have greater knowledge of the psychology of the laboratory rat than we have of the psychology of human beings. Psychological studies, although not as extensive as in the case of the rat, have been undertaken on other animals in current laboratory use—for example, mice, cats, dogs, and monkeys.

Department of Psychology, University College London, London, W.C.1. R. H. J. WATSON.

ORAL TREATMENT OF PERNICIOUS ANÆMIA

SIR,—In recent work of ours on the intrinsic factor activity of human gastric juice, after its fractionation by continuous electrophoresis,[1] the conclusion was drawn that there are no valid reasons why intrinsic factor should be necessarily thought of as a definite substance rather than as a reactive or prosthetic group contained in materials with intrinsic-factor activity. This reactive group could be present either in various mucoproteins of gastric juice, at various concentrations, or in one mucoprotein only and its degradation products. There is still a big step from this new concept to Dr. Heathcote and Dr. Mooney's suggestion, according to which an active vitamin-B_{12}-peptide complex, absorbable in the intestine, is produced in the normal stomach by simple proteolysis of vitamin-B_{12}-protein compounds, and that the intrinsic factor, in all probability, does not exist at all.[2]

The following comments on this work occur to me:

(1) It would be preferable that the potency of Dr. Heathcote and Dr. Mooney's vitamin-B_{12}-peptide complex be evaluated by the currently accepted methods, which include: (*a*) testing the preparation by the method of hæmatopoietic response on the part of patients with pernicious anæmia in relapse, at a vitamin-B_{12} dose level not exceeding 15 μg. per day,[3] with a preliminary period of ten days during which a similar dose of vitamin B_{12} alone is given by mouth as control; (*b*) testing the preparation by one or more of isotope techniques such as the urinary [4] or fæcal [5] excretion tests, measurement of the hepatic uptake of radioactivity,[6] or determination of blood radioactivity [7 8] following administration of a labelled vitamin-B_{12}-peptide complex in which vitamin B_{12} may be tagged with ^{56}Co, ^{58}Co, or ^{60}Co.

(2) It would be good to ascertain, by any one of the just-mentioned isotope techniques, that the cases used by Dr. Heathcote and Dr. Mooney do not represent nutritional vitamin-B_{12} deficiency. The latter can be clinically and hæmatologically indistinguishable from pernicious anæmia,[9] but would, of course, respond readily to the oral administration of any material which contained appreciable amounts of vitamin B_{12}.

(3) The proof of the satisfactory maintenance of pernicious-anæmia patients on Dr. Heathcote and Dr. Mooney's preparation would be better supported by:

(*a*) Extension of the maintenance treatment of patients with pernicious anæmia beyond the period of 140–290 days reported by the authors. A remission of 5 to 10 months' duration after an oral dose of 1500 μg. vitamin B_{12} during the first 3 weeks of treatment may not be surprising at all. Moreover, it would be of interest to demonstrate the superiority of Dr. Heathcote and Dr. Mooney's treatment over the conventional oral treatment of pernicious anæmia with commercially available intrinsic-factor preparations. The resistance to orally administered commercial intrinsic factor develops rather late in the course of the conventional oral treatment.[10 11] The

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observation periods in Dr. Heathcote and Dr. Mooney's cases are probably not long enough to make sure that a similar resistance will not develop vis-à-vis the vitamin B_{12}-peptide complex.

(*b*) Measurement of vitamin-B_{12} levels in the blood during the entire treatment period. It would be worth while to know whether patients on vitamin-B_{12}-peptide oral treatment can maintain satisfactory vitamin-B_{12} blood-levels for a reasonable time.[12]

Let us now assume that the vitamin-B_{12}-peptide complex has satisfactorily met all these requirements and that its potency has been established beyond doubt. Still, the concept of gastric proteolysis as the key to the understanding of vitamin-B_{12} absorption and pathogenesis of pernicious anæmia will require some reconciliation with the information available on the digestive and absorptive processes in the gastrointestinal tract. The following questions require answers:

(1) If defective proteolysis in the stomach is the main factor in pernicious anæmia responsible for the defective intestinal absorption of vitamin B_{12}, then why would not trypsin, chymotrypsin, and all the potent intestinal peptidases take over the function of the defective or absent proteolytic enzymes of the stomach? It is well known that these enzymes can digest any other proteins of food in the absence of gastric secretion. Why should they not digest the vitamin-B_{12}-protein compounds and transform them into a vitamin-B_{12}-peptide complex absorbable in the lower ileum?[13] The earlier concept of Cheney—that trypsin is absent in pernicious anæmia [14]—has been long since disproved [15] and it is well known that the proteolytic enzymes of the pancreas are secreted in pernicious anæmia, although often in decreased amounts.

(2) Why do most of the patients with simple histamine-fast anacidity show an entirely normal intestinal absorption of vitamin B_{12} in the intestine, as determined by assay with labelled vitamin B_{12}? [16 17] In most of these patients the gastric proteases (pepsin and cathepsin) are absent,[18] and one would expect that the conversion of vitamin-B_{12}-protein to vitamin-B_{12}-peptide in the stomach would be similarly impaired. Otherwise, one would have to admit the existence of some additional unknown proteolytic factor in the stomach of normals and patients with simple histamine-fast anacidity and its absence from the stomach of patients with pernicious anæmia. Since this factor is as yet unknown, one could apply to its hypothetical existence the same criticism which Dr. Heathcote and Dr. Mooney apply to the existence of intrinsic factor and an intestinal vitamin-B_{12} acceptor.

(3) Why do juvenile patients with pernicious anæmia show defective intestinal absorption of vitamin B_{12} on isotope tests and hæmatological assays, and develop pernicious anæmia although the gastric secretion of free hydrochloric acid, pepsin, and cathepsin is for the most part in a normal range? [19 20] The hypothetical mucolytic enzyme mucolysine,[21] which splits visible mucus into mucoproteose, appears also to function normally in these patients, since the concentration of mucoproteose in their gastric juice is normal.[22] If the abnormal proteolysis in the stomach should be the key to the problem, how can one explain the defective absorption of vitamin B_{12} in these patients and its correction by the addition of normal human gastric juice or animal intrinsic factor preparations?

(4) Referring to the concept of active vitamin-B_{12}-peptide complex, Dr. Heathcote and Dr. Mooney state: "On this theory, extrinsic and intrinsic factors are no longer necessary; nor is the third factor of Glass, because this 'free' form of the vitamin will be of a suitable size for simple absorption in the small intestine." If this is so, why, then, is the intestinal absorption of vitamin B_{12} sharply limited, as well, under normal conditions? [23] How can the concept of proteolysis of a vitamin-B_{12}-protein compound explain the regression of absorption of vitamin B_{12} in the normal intestine on increase of the dose? On the existence of this regression, everyone agrees.[24 25] With adequate proteolysis in the normal stomach, there is obviously no reason for this phenomenon. The formation of vitamin-B_{12}-peptide complex in the stomach and its free passage through the intestinal wall would be secured by normal gastric proteolysis.

I feel sure that Dr. Heathcote and Dr. Mooney will be able to supply answers to these questions. This will be in the interests of all who, like myself, are intrigued by the freshness and potentialities of the concept of defective proteolysis in the pathogenesis of pernicious anæmia.

Department of Medicine,
New York Medical College,
Flower and Fifth Avenue Hospitals,
New York, N.Y. GEORGE B. JERZY GLASS.

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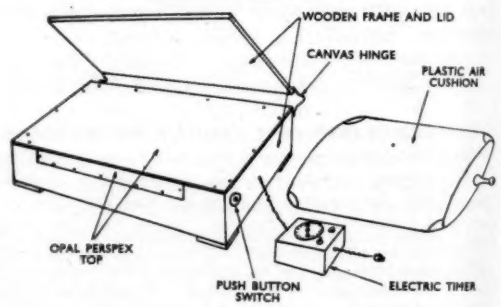
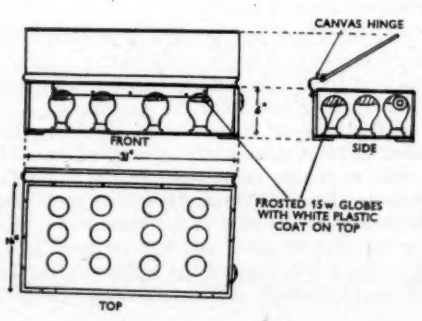
AN INEXPENSIVE PHOTOCOPYING UNIT

SIR,—A departmental photocopying unit has proved of advantage in that reprints are immediately available for teaching and research purposes. The unit consists of a contact printer, an air cushion, and a timer, visual or electric.

The contact printer, made of box wood, is 21 in. × 16 in. × 6 in., contains 12 15-watt frosted globes, and is covered by an opal 'Perspex' top. A strip of opal perspex is set in the vertical front to allow the centre margin of bound volumes to be in contact with the light and not obscured by the width of a vertical margin of wood; the volume is photographed 1 page at a time.

The inside of the contact printer and the top of the frosted globes are painted with a quick-drying white plastic paint to give more even lighting to the perspex top.





A wooden lid hinged on canvas is used for pressure, which is evenly distributed by means of an air cushion of plastic 20 in. × 15 in. × 5 in.

An electric timer is preferable, but the printer can be used with a watch or laboratory timer and a push-button switch.

When developing the prints the usual darkroom equipment —namely, two developing trays, print dryer, and safety light— are necessary. The photographic paper used is copy rapid negative paper ('Agfa'), and the developer and fixative used are copy rapid developer and 'Amfix' ultra-rapid hardener.

The following method of printing has been found to be quick and economical. The journal, book, or article is laid face down on the contact printer with the photographic paper emulsion side up between the perspex top and the page to be copied. The journal or book is pressed on to the paper by means of the air cushion and manual pressure applied on the lid. The light is switched on for 3 seconds and the paper removed for developing. This is done by placing the paper on a piece of glass or perspex, and the Agfa copy rapid developer is wiped on with a sponge; the image appears instantly. It is then wiped with water followed by fixative and washed before placing on the dryer. This takes approximately 1 minute, and drying takes 1–3 minutes.

The negative is now ready for reversal to positive image. Using the same Agfa copy rapid negative paper, it is placed emulsion side down on to the dry negative, which is placed face up on the printer, and the air cushion keeps the two pieces of paper in close contact. The light is switched on for approximately 20 seconds; the paper is removed for developing, using the same procedure but allowing the positive copy to stay in the fixative from 5 to 10 minutes before washing and drying.

The cost of the page, depending on the size, is approximately 6–10*d*. the latter for foolscap size.

The materials for the contact printer cost between 30*s*. and £5, excluding the electric timer and darkroom equipment.

Department of Surgery,
University of Natal,
Durban.

A. E. KARK
C. J. LOCKETT.

CHLORPROPAMIDE

SIR,—In view of the encouraging results which we obtained with chlorpropamide it is disappointing to learn that Dr. Joan Walker (Sept. 20) has had such unfortunate experience with the drug. Although, apart from her initial trial with 1·5 g. daily, the dosage she employed was low (0·2–0·5 g.) we believe that the occurrence of unpleasant side-effects is most probably attributable to the amount of the drug administered.

Dr. Walker maintained the blood-sugar at a satisfactory level in 38 (88%) of her cases, a response much better than in our series in which only 65% were successful. The 13 cases maintained on 0·5 g. or less she believes "may eventually be controlled on diet alone". It seems possible that Dr. Walker persists with the drug when we would have abandoned it, and consequently has given larger total doses to individual patients. We have always endeavoured to give the smallest possible amounts of the sulphonylureas, and with our method of intermittent use of these drugs, as reported at the International Diabetes Federation meeting in Dusseldorf, the drug is discontinued after a satisfactory response has been obtained and not started again until the reappearance of glycosuria seems to make this desirable.

Our present method of using chlorpropamide is to give it only to such patients as experience has shown to be most likely to prove responsive, the initial dose being 1 g. at breakfast-time. If after four days satisfactory control has not been obtained the patient is regarded as "unresponsive" and the drug abandoned. Often, however, the response is dramatically quick, and the dose is then immediately reduced to 0·5 g., to be further reduced to 0·2–0·25 g. after a few days if satisfactory control continues. The initial course of treatment is for fourteen days. Should glycosuria recur, as it may do after an interval of perhaps two to three weeks, the drug is started again in a dose of 0·2–0·5 g. daily. With this regime we have had no evidence of significant toxic effects. Nevertheless chlorpropamide is a powerful hypoglycæmic agent, considerably more potent than tolbutamide, and we are continuing our investigations to discover the lowest dosage in which it may prove effective.

We are interested to note that in 4 of Dr. Walker's cases intercurrent infection or other illness resulted in chlorpropamide becoming ineffective.

We have previously reported this lapse from control, both with carbutamide and tolbutamide, and the situation seems comparable to the increased requirements, under such circumstances, of the patient taking insulin.

IAN MURRAY
M. J. RIDDELL
IAN WANG.

Victoria Infirmary, Glasgow.

SIR,—Dr. Walker reports an unusually large number of side-effects with chlorpropamide ('Diabinese') in the treatment of diabetes mellitus. This letter serves a most useful purpose because it shows the importance of dosage.

When we began our first trials with chlorpropamide, we did not know that it was such a potent drug; therefore we all used too large a dose. However, the side-effects from an excessive dose no more contraindicate its use in diabetes than does the vomiting produced by too large a dose of digitalis suggest that the drug should not be used in heart-disease.

I have checked the progress of all the patients that I treated with chlorpropamide in Galway with a series of four-hourly blood-sugar estimations. As an article to appear in the *Journal of the Irish Medical Association* will show, I have found that chlorpropamide is the most satisfactory oral antidiabetic drug so far available. It is more potent and, when the correct dose is given, it is less toxic than carbutamide. It is much more potent than tolbutamide, and it need not be given so frequently.

As I said at the International Diabetes Federation meeting in Dusseldorf, it is very important to begin with a small dose (0·25 g. daily), just as we begin with a small dose of insulin. If necessary, the dose may be increased every five days by 0·25 g. to a maximum of 1 g. In some patients, one must reduce the maintenance dose again later to as low as 0·1 g., just as one must frequently reduce the dose of insulin after a while.

I have now treated 20 diabetics with chlorpropamide using this system of dosage and only 1 of them has complained of any serious side-effects. This man is an alcoholic. He complained of dizziness and tachycardia when he drank half a glass of Irish whiskey. He says he has not taken a drink since. Thus, not only has the drug controlled his diabetes, but it has also apparently cured his alcoholism.

Galway Regional Hospital. B. J. O'DRISCOLL.

REACTION TIME IN MYXŒDEMA

SIR,—In estimating the reaction time in myxœdema (the subject of Dr. Murray's article of Aug. 23) a simplified method is to use two stop-watches.

A small dry battery and a lamp are connected with one of the watches in such a way that the lamp lights whenever the button is pressed. The two watches are started simultaneously. The observer keeps the one with the lamp attached, the other one is given to the patient. The patient is now asked to press the button on his watch as soon as he sees the lamp light. The difference in the time readings of the two watches immediately gives the reaction time.

Indre Hardanger Sjukehus,
Odda, Norway. ERIK MAGNUS.

X-RAY CONTRAST-CONVERSIONS WITH TELEVISION: A MEANS OF REDUCING EXPOSURE OF PATIENTS

SIR,—In a closed television system, single X-ray films may be scanned by means of a flying-spot cathode-ray tube and the image displayed on a monochrome television monitor. By the incorporation of special circuits, we are able to increase the contrast by progressive steps beyond the range of the ordinary television receiver.

The film is scanned 30 times a second by a rectangle of light 3 × 4 in. having 525 lines. This rapidly moving spot of light is imaged by means of a lens on to a 6 × 8 in. area of the X-ray film. By clipping steps of luminance beyond the area under analysis and expanding the remaining narrowed portion of the brightness band to the full original dynamic range of contrast, areas 2% or less in contrast differences can be made perceptible. The horizontal resolution of the system is approximately twice as great as American commercial television, not being limited to a 4-megacycle channel; and the signal-to-noise ratio is much higher.

With the use of this equipment, a radiologist can view a single film with many progressive contrast conversions, such as are indicated in figs. 1–5. Thus, a patient is spared multiple exposures. Simultaneously, the radiologist has brought to his attention adjacent areas of poor contrast by the increased enhancement and is spared the chagrin of overlooking important diagnostic details.

The luminance in reading X-ray films ranges from a fraction to about 150 foot-lamberts, so that contrast differences of less than 2% usually escape the radiologist's attention. These small differences are much increased by

Fig. 3—With additional clipping and expansion, as shown in fig. 2, the soft tissues of the posterior tongue, epiglottis, larynx, and posterior neck have been brought into view.

Fig. 1—Televised view of a film, a lateral projection of the cervical spine with no contrast changes from the original.

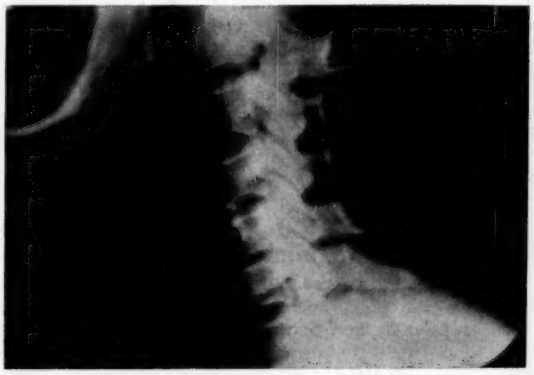


Fig. 4—By reverse clipping to that shown in figs. 2 and 3, and expansion to the full dynamic range of the television system, the denser bony structures of the cervical spine are now displayed.

Fig. 2—By slight clipping of luminance in the dark areas and with re-expansion to the dynamic range of the television system, the soft tissues in the hypopharyngeal and œsophageal areas have been brought into view.

Fig. 5—With more clipping than in fig. 4, all the structures except the cervical articulations are blotted out of view so that the cervical joints now are more clearly visible than on the original film.

our television techniques so that many abnormal changes, otherwise unnoticed, quickly become discernible.[1–3]

Department of Radiology, Albert Einstein Medical Center, Philadelphia. J. GERSHON-COHEN.

Research Department, Philco Corporation, Philadelphia. J. F. FISHER.

MALIGNANT RENAL HYPERTENSION CURED BY NEPHRECTOMY

SIR,—I was sorry to see that the report by Dr. Peabody and Dr. Gates (Aug. 9) of a case of hypertension cured by nephrectomy included no reference to the pioneers in such an exciting clinical experience. The first such case was reported by Butler [4] from Harvard in 1937. This account was quickly followed by a similar report by Leadbetter and Burkland [5] from Johns Hopkins.

Boston, Mass. EARLE M. CHAPMAN.

ACCIDENTAL HYPOTHERMIA

SIR,—I was interested to read Dr. Moylan's letter (Sept. 20) describing hypothermia complicating schizophrenia, as a similar case was seen at this hospital last March, when the weather was unusually cold.

The patient was a thin, ill-kempt, louse-infested man of 52 who was stuporose, the only history then available being that he had been found unconscious at home that morning, March 20.

Rectal temperature 73°F (22·8°C), pulse rate 32, respiration-rate 14, and blood-pressure 80/? mm. Hg. He felt cold, and all limbs were stiff, although he made occasional gross movements. The right testicle was retracted to the external ring. Tendon reflexes present. Pupils dilated, and reacted very slowly, taking about 15 sec. to contract on illumination, and as long to dilate again. Heart-sounds were faint, and the 1st and 2nd sounds wide apart. There were small ulcers on the nose and legs, and herpes labialis. No signs of myxœdema or of hypopituitarism were found.

Investigations.—E.C.G. typical of hypothermia, with marked slowing of the ventricular complexes, and J-wave present in V_5. Basal metabolic rate 46%. Urine normal. Serum-cholesterol 118 mg., blood-urea 63 mg., blood-sugar 84 mg. per 100 ml. Hæmoglobin 97% (14·4 g. per 100 ml.). Erythrocyte-sedimentation rate normal.

His temperature was slowly raised with an electric blanket, and after 5 hours he began to twitch or shiver, and the pupils were noticed to react fairly quickly, his temperature then being 82° F (27·3°C). 15 hours after admission, when his temperature was 93°F (33·9°C), he suddenly developed pulmonary œdema and soon died.

Necropsy by Dr. A. Levene showed bilateral basal bronchopneumonia, with superadded pulmonary œdema, as the immediate cause of death. There was also a healing ulcer on the lesser curvature of the stomach. No evidence of endocrine dysfunction was found.

The sequence of events was reconstructed as follows. 3 days before admission he felt weak and had a cold. He stayed alone in his unheated home, being unable to summon help. The illness progressed to bronchopneumonia, and a combination of this, his previous self-neglect, chronic schizophrenia, poor nutrition, and the cold weather caused the hypothermia.

I am grateful to Dr. K. O. Rawlings, under whose care the patient was admitted, for permission to publish this case, to Dr. A. Levene who performed the necropsy, and to Dr. L. A. Laventhall, the patient's own doctor, whose inquiries made the reconstruction of events possible.

Beckenham Hospital, Beckenham, Kent. G. J. ROCKLEY.

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INDUSTRIAL MEDICINE AND GENERAL PRACTICE

SIR,—The criticisms by certain whole-time industrial medical officers of the one-line quotation in *The Times* from an article of mine in *The Practitioner* are reasoned and reasonable. No-one who knows industry will deny the importance of the study of the relationship between the individual and his working environment, in both health and disease. Again, Dr. Herford (Sept. 20) has my full support in his plea for a regional occupational hygiene laboratory service.

But the industrialist still requires first that his work-people should be looked after efficiently and swiftly when they are injured or taken ill at the place of work, and this really is general practice in an industrial context. It is only when his medical department or industrial health service has convinced him of its therapeutic competence that the industrialist will treat seriously its advice on prevention and positive health.

Moreover, the good G.P. is as much concerned with the patient's working environment as the industrial medical officer, though unfortunately he may know much less about it. It is he, and not the I.M.O., who has to order the patient off, or back to, work. I know from experience that he does this much more intelligently if he holds a part-time industrial appointment.

It would be a bad thing for industry and medicine if the idea got abroad that there is some kind of conflict between the whole-time and part-time I.M.O.s. To save further misunderstanding, may I quote the two paragraphs from which *The Times* extracted part of a sentence:

> " Good general practice is essentially good medicine, wherever it is conducted. A large part of industrial medicine is neither more nor less than general practice, conducted in the context of the factory or other work-place. But this is not the whole story. An analogy may be drawn between industrial medicine and obstetrics. A large part of obstetrics is properly done by general practitioners, and the good general-practitioner obstetrician reaches a high level of technical skill. But he does not, and should not, replace the specialist obstetrician, although their spheres of action will sometimes overlap. No matter how large a part the general practitioner comes to play in industry, we shall still need specialists in industrial medicine: to investigate toxic hazards, new and old, to advise on the difficult cases, to conduct research and to organize and develop within industry the health services which may be needed.
>
> " There is no need for antagonism between the general practitioner in industry and the whole-time industrial medical officer. The latter has a duty to make himself a specialist in his subject. How much he has already achieved may be judged from the pages of the *British Journal of Industrial Medicine* and the *Transactions of the Association of Industrial Medical Officers*. It is to be hoped that, increasingly, whole-time industrial medical officers will call in local general practitioners as working members of their departments—not as assistants, but as full clinical colleagues on a part-time basis. Each will learn much from the other, and industry as a whole will benefit."

In industry, there is not only room for the G.P., and the whole-time industrial medical officer; there is need for both of them.

Harlow. TAYLOR.

CORTISONE IN THE TREATMENT OF ACUTE INFECTIONS

SIR,—Like Dr. Breen,[1] I have found cortisone often very useful in the treatment of acute infections.

In the past ten years over 14,000 patients of all ages have been treated at the infectious-diseases clinic of the Medical Academy in Gdańsk (Danzig). In 1951 we introduced hormone therapy for those with signs of shock—i.e., those showing collapse (sometimes from vomiting or diarrhœa) or hæmorrhages. Here the early use of cortisone—before an antibiotic is given—has proved a lifesaving first-aid procedure. Antibiotics cannot

1. Breen, G. E. *Lancet*, 1958, i, 589.

combat the state of shock, and may sometimes cause additional stress. We have already used cortisone in more than 150 cases without serious side-effects, and we think that many lives have been saved by it.

In addition, we have seen benefit from cortisone in more than 100 cases of so-called hypertoxic diphtheria or of severe purulent meningitis (coccal or tuberculous) in which the prognosis often seemed hopeless. In some of these there was a spectacular improvement—never seen to the same degree with antibiotic treatment alone.

The dose of cortisone in the acute infections was rarely more than 300 mg. in children and 800 mg. in adults; in hypertoxic diphtheria and in meningitis it averaged 600 mg. in children and 1000 mg. in adults.

In virus hepatitis, if the case is taking a turn for the worse, we give corticotrophin by continuous drip. This has been necessary in about 15% of our cases (now numbering nearly 2000), and about 30 needed cortisone (or prednisone) too. Very occasionally we have used cortisone without giving corticotrophin first. Only one of our patients has gone into coma. Some of those who were in coma on admission have recovered after cortisone given with glucose and an antibiotic of the tetracycline group. The antibiotic does not, we think, affect the virus but may reduce formation of ammonia in the intestine.

Medical Academy, Gdańsk (Danzig), Poland.

VICTOR BINCER
Professor of infectious diseases and epidemiology.

THE FRONTIERS OF MEDICINE

SIR,—Dr. Robert Marshall (Sept. 20) read into a sentence of my essay an insult which was certainly not intended. The statement to which he took exception was certainly a correct version of at least one section of student opinion. Nor do I think the opinion to be one confined to the period of my own training. It is very likely that my own students comment in similar terms at the impotence of physicians to halt the progress of emphysema or of bronchial carcinoma.

Perhaps Dr. Marshall cannot believe that the successes of which we may justly be proud are less impressive to the young than are our failures. I believe this to be the case, however, and instead of being insulted by student criticism we should be stimulated and invigorated by it. In this sense at least I am sure that my opinions will be shared by many academic colleagues in this country and perhaps abroad.

The Royal Hospital, Sheffield.

C. H. STUART-HARRIS.

ORAL IRON PREPARATIONS

SIR,—Sir Stanley Davidson and Dr. Richmond (Sept. 13, p. 570) recommend ferrous-sulphate tablets as the preparation of first choice for oral iron therapy, but report that organic preparations are prescribed much more frequently. One reason for this may be the publication of a number of reports [1–20] of accidental poisoning by ferrous sulphate, which in 1950 displaced strychnine as the commonest form of fatal poisoning among children in this country.[21]

Several preventive measures have been suggested, such as incorporating a small dose of an emetic in the tablets, dispensing them in screw-capped bottles or in 'Cellophane' strips, and including them in the Poisons List; but fatalities continue to occur [22], and under present circumstances it would appear quite justifiable not to prescribe tabs. ferri sulph. for use in the home.

Oxford. K. W. LOVEL.

DIASTOLIC PRESSURE AND MALIGNANT HYPERTENSION

SIR,—Dr. Stewart (Aug. 16) states: "The malignant phase bears no direct relationship with the pressure itself. A diastolic reading of 110 may be accompanied by a malignant fundus in an eclamptic young woman, while in a man of sixty a diastolic level of 150 may have produced only the earliest retinal changes."

Here in Chile we accept the theory of Pickering [23] that an established high diastolic pressure is the cause of the malignant phase of hypertension. This theory has saved many lives in our hospital in the last five years. We have many patients with malignant hypertension who are alive after three to five years (according to Kincaid-Smith et al.[24] 90% of untreated patients with malignant hypertension die within a year). Our patients received treatment to lower their high diastolic pressure, and with lowering of the pressure the malignant fundus has become non-malignant. The overall mortality of 439 hypertensive women, with a mean age of 47·5±8·7 years, studied over a period of eight years before the era of the ganglion-blocking drugs, in the National Service of Preventive Medicine in Santiago,[25] is 33·3% in the group with diastolic readings over 120 mm. Hg, and only 4·4% in the remainder. The level of the diastolic pressure is directly related to mortality.

If we apply the table of the diastolic age-sex-adjusted score of Pickering (D.A.A.S.) to these two cases it is possible to understand the paradox mentioned by Dr. Stewart. The young woman (perhaps 20 years old) has a D.A.A.S. of 70 mm. Hg and the man of 60 has a D.A.A.S. of only 60 mm. Hg. In relation to age and sex, the young woman has a greater "degree of deviation" of her pressure than the man of 60. A diastolic reading of 110 mm. Hg is very severe in a girl of 20 because her D.A.A.S. is very high; but the same reading in a man of 60 is without importance (D.A.A.S. very low). The explanation of why the man with a diastolic pressure of 150, or a D.A.A.S. of 60, has a non-malignant fundus is as follows: the quantitative component of the diastolic pressure has two factors—intensity and velocity of increase of pressure—and the malignant phase is entered only if there is a high level of intensity at a high velocity of increase of pressure. We have observed, studying the rate of increase of pressure in relation to age in patients with hypertension, that the velocity of increase of pressure declines with advancing age.[26] Thus a patient with high intensity, but 60 years old, has a low velocity of increase of pressure, and malignant hypertension is much less liable to develop than in a younger person. This is an explanation of why malignant hypertension does not appear in older patients.

In my earlier letter (July 26) I said that with the D.A.A.S. scale it is possible "to identify patients with malignant hypertension before changes are evident in the fundus", because in the classification of our patients with the D.A.A.S. scale we have 16·6% of patients with a normal fundus in the highest "degree", whereas in the classical scale we have not a single

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25. Viel, B., Castro, V. Tesis de Medico Cirujano, Facultad de Medicina, Universidad de Chile. 1952, **1**, 211.
26. Cruz-Coke, R. Velocity and Acceleration of Diastolic Pressure. To be published.

patient with a normal fundus in the highest level of 160 mm. Hg and over, and in the two scales the highest degree has the greatest percentage of malignant cases. When we first assess a new patient with hypertension and we find a D.A.A.S. of 75 mm. in two or more examinations, we can presume that the patient is entering the malignant phase, before we examine the fundus. With a D.A.A.S. of 75 mm. this patient has 16% of probability of having a normal fundus, showing that he is in the incipient period; and he has 46% probability of having a malignant fundus, showing that he is in an advanced stage.

With this method it is possible to make more accurate the quantitative diagnosis of hypertension. Individual prognosis must be considered according to: (1) quantitative diagnosis with the D.A.A.S. scale, (2) the ætiology of the hypertension, (3) environmental factors, and (4) the extent of the genetic factor in the arterial pressure of first-degree relatives of the patient.

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Aguirre Hospital,
University of Chile, Santiago. RICARDO CRUZ-COKE.

COMBINED GASTRIC AND DUODENAL ULCER

SIR,—Data from many countries have shown that there is an excess of individuals of blood-group O amongst subjects who have duodenal ulcer; and in those who have gastric ulcer there is also an excess of individuals of blood-group O, but to a significantly smaller extent. The situation with combined gastric and duodenal ulcer has not been mentioned specifically and data are available [1-4] from which it is possible to compare the ABO blood-group distribution between combined ulcer and gastric and duodenal ulcer separately. It has been impossible to make separate calculations for each sex.

Tables I and II show an analysis of these data, including material from Sydney accumulated from hospital inpatient records during the period 1945–55. With combined gastric and duodenal ulcer the pattern of the ABO blood-groups is similar to that found with duodenal ulcer alone and differs significantly from that found with gastric ulcer alone.

It has been suggested that in gastric ulcer the relationship to the ABO blood-groups is concerned with intragastric site,[5 6]

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TABLE I—COMPARISON OF ABO BLOOD-GROUP DISTRIBUTION BETWEEN GASTRIC ULCER AND COMBINED GASTRIC AND DUODENAL ULCER (351 CASES FROM 7 SOURCES)

Place	Authority	Type of ulcer	Total	O	A	B	AB	$\frac{A}{A+O}$	Difference between gastric and combined ulcer*: weight
London, Manchester, Newcastle	Aird et al.[1]	Gastric	1015	538	376	77	24	0·4114	6·728
		Combined	113	63	41	4	5	0·3942	
Glasgow	Peebles Brown et al.[2]	Gastric	300	174	90	27	9	0·3409	9·939
		Combined	38	24	9	5	0	0·2727	
Liverpool	Clarke et al.[3]	Gastric	438	215	179	33	11	0·4543	27·249
		Combined	48	30	13	4	1	0·3023	
Iowa	Buckwalter et al.[4]	Gastric	469	248	183	26	12	0·4246	6·966
		Combined	69	37	24	6	2	0·3934	
Sydney	Present series	Gastric	961	473	375	83	30	0·4422	47·895
		Combined	83	51	21	8	3	0·2917	

* $\chi^2 = 7{\cdot}75$. n = 1. $P < 0{\cdot}01$.

TABLE II—COMPARISON OF ABO BLOOD-GROUP DISTRIBUTION BETWEEN DUODENAL ULCER AND COMBINED GASTRIC AND DUODENAL ULCER (351 CASES FROM 7 SOURCES)

Place	Authority	Type of ulcer	Total	O	A	B	AB	$\frac{A}{A+O}$	Difference between duodenal and combined ulcer*: weight
London, Manchester, Newcastle	Aird et al.[1]	Duodenal	1851	1048 (56·6%)	616	141	46	0·3702	−10·836
		Combined	113	63 (55·8%)	41	4	5	0·3942	
Glasgow	Peebles Brown et al.[2]	Duodenal	1642	947 (57·7%)	517	145	33	0·3531	+13·033
		Combined	38	24 (63·2%)	9	5	0	0·2727	
Liverpool	Clarke et al.[3]	Duodenal	1059	631 (59·1%)	307	86	35	0·3272	+4·864
		Combined	48	30 (62·5%)	13	4	1	0·3023	
Iowa	Buckwalter et al.[4]	Duodenal	1301	698 (53·7%)	472	102	29	0·4034	+2·428
		Combined	69	37 (53·6%)	24	6	2	0·3934	
Sydney	Present series	Duodenal	192	130 (67·7%)	46	12	4	0·2614	−7·639
		Combined	83	51 (61·4%)	21	8	3	0·2917	

* $\chi^2 = 0{\cdot}0026$. n = 1. $P > 0{\cdot}95$.

TABLE III—CHRONIC GASTRIC ULCER: SITE OF 1569 ULCERS IN 1496 PATIENTS (SYDNEY 1945–55)

Site	No duodenal ulcer		With duodenal ulcer		Total	
	Male	Female	Male	Female	Male	Female
Prepyloric ..	294 (36·2%)	137 (21·3%)	14 (19·7%)	9 (20·9%)	308 (34·8%)	146 (21·3%)
Fundic ..	504	497	57	34	561	531
Cardiac ..	15	8	..	..	15	8
Total ..	813	642	71	43	884	685

lesions in the prepyloric region showing an excess of group A, and those in the fundic region an excess of group O. Table III, derived from the Sydney material, appears to indicate that in men, but so far not in women, the proportion of gastric ulcers in the fundic region is increased in the presence of an associated duodenal ulcer. It is not clear whether this is a true sex difference. With gastric ulcer alone, women in Sydney and elsewhere have significantly more fundic ulcers than men, and indeed also show a higher proportion of individuals of blood-group O.[7]

Gastrointestinal Clinic,
Sydney Hospital, New South Wales. B. P. BILLINGTON.

INTRA-ARTICULAR HYDROCORTISONE

SIR,—Dr. Chandler and Dr. Wright (Sept. 27, p. 661) perform a valuable service in drawing attention to certain dangers inherent in the use of intra-articular hydrocortisone in weight-bearing joints, and in so doing they underline the common experience of those who specialise in the management of rheumatic disorders. Many doctors unfortunately seem to regard the intra-articular use of steroid preparations as a panacea, and it is well that they should be reminded that this method of treatment can only prove effective in the long run if it is employed as part of a carefully planned therapeutic regime.

Careful examination of an actively inflamed knee-joint will reveal a loss of quadriceps power and bulk, the degree of which

7. Billington, B. P. Proceedings of the World Congress of Gastroenterology, 1958 (in the press).

varies directly with both the duration and severity of the inflammation. With the sudden loss of pain attendant upon the halting of the inflammatory process by the steroid preparation, the joyful owner of the knee is immediately emboldened to exploit its apparently increased exercise tolerance long before the joint is structurally ready to contend with the strains imposed. Patients must be kept under close observation and instructed to live within the limits imposed by their muscular deficit. The potential danger is increased in so far as it is often hard to convince the patient that weight-bearing activity must be very carefully graduated whilst rehabilitation of knee function is slowly progressing. Usually this restoration of function can only be achieved by a combination of physical and other methods of treatment, in which the proper use of intrasynovial steroids plays a valuable part.

Clearer thinking in this matter might be engendered if it was more generally appreciated that the sole action of hydrocortisone and other steroids at the point of local application is the damping down of the non-specific inflammatory response.

St. Thomas's Hospital, London, S.E.1. D. R. L. NEWTON.

PAPA VIRCHOW

SIR,—Professor Johnston (Sept. 27, p. 701) traded his Liddell and Scott for Gray. What have you traded your Lewis and Short for? There is no such Latin word as *cellule* and I am sure Papa Virchow knew it.

London, W.1. JOHN PENMAN.

MECAMYLAMINE AND THE NERVOUS SYSTEM

SIR,—Treatment with mecamylamine has sometimes caused tremor, anxiety, and (later) psychosis.[1–4] This syndrome has usually arisen after large doses, and has quickly disappeared on withdrawal of the drug. In the following case it developed with a smaller dose and has persisted for over a year.

In August, 1955, a man aged 49 complained of recently impaired vision, headaches, and vomiting. His blood-pressure was 240/140 mm. Hg. (At a routine examination in March, 1954, it had been 220/130 but no treatment had been advised.) There was bilateral papillœdema with hæmorrhages. The blood-urea level was 31 mg. per 100 ml. and there was slight albuminuria. Severe essential hypertension was diagnosed.

During the next year he was admitted to hospital several times, but he insisted on working as much as possible because he had a family to support. With alseroxylon (' Rauwiloid ') the blood-pressure fell to 190/110, but it soon rose again. When pentolinium (' Ansolysen ') was given by mouth he often collapsed, the blood-pressure on one occasion being 90/60. Between the hypotensive episodes the figures were around 230/130. The retinopathy waxed and waned.

On Aug. 30, 1956, treatment was started with mecamylamine 7·5 mg. daily, increasing gradually. The blood-urea level was 32 mg. per 100 ml. Five weeks later, when having 15 mg. of mecamylamine daily, he was seen to be shaking. The tremor was coarse, and more rapid than is usually seen in parkinsonism, and it involved all the body. The tendon reflexes were brisk, and no other neurological abnormality could be demonstrated. The blood-pressure was 250/130. The dose of mecamylamine was increased to 20 mg. daily. After ten days, when the blood-pressure was 210/125, he developed ill-founded worries and feelings of guilt, and an obsession compelling him to wash his hands continually.

On Dec. 10, 1956, he complained of more severe headache, and his blood-pressure rose to 230/155. The dose of mecamylamine was again increased—to 30 mg. daily. Two days later he became confused and irritable; the blood-pressure was 220/130 and the blood-urea level had risen to 108 mg. per 100 ml. On readmission to hospital he became unmanageable and violent. He was transferred to the observation ward, certified, and removed to a mental institution, where he remained until his death in April, 1958, though he improved sufficiently to sign voluntary-patient documents last December. In March, 1958, he was having reserpine (' Serpasil ') 1 mg. b.d., and the blood-pressure was around 160/100. He was fairly demented, with slow cerebration, though he was pleasant, cooperative, and an excellent ward worker. He died suddenly on April 7, 1958. Necropsy showed the cause of death to be an extensive coronary infarction. Considerable cerebral atheroma was present.

This patient developed a tremor when receiving only 15 mg. of mecamylamine daily, and became psychotic within three days of the dose being increased to 30 mg. daily. His later course suggests that it would be wise to abandon treatment with mecamylamine as soon as any patient shows anxiety and tremor. The association of a rising blood-urea level with the onset of psychotic symptoms fits in with the suggestion [3] that the psychosis is related to retention of mecamylamine, excretion of this drug being reduced in renal failure.[5]

I should like to thank Dr. G. B. Hollings for his advice and help with this case, Dr. D. Stark Murray for the pathology reports, and Dr. C. Milne for the psychiatric report.

New Malden, Surrey. GORDON HICKISH.

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Appointments

DONALD, D. E., M.B. Glasg., D.P.H.: deputy M.O.H., principal school M.O. and port health M.O., Swansea.
DUNNE, HELEN M., L.R.C.P.I., D.P.H.: assistant M.O., Beckenham area, Kent.
ESSEX-CATER, A. J., M.R.C.S., D.P.H., D.C.H., D.I.H.: administrative M.O.H., Birmingham.
GILLANDERS, L. A., M.B. Glasg., F.F.R., D.M.R.D.: part-time consultant radiologist, Aberdeen general and special hospitals.
HARRISON, MARION, M.B. Durh., D.P.H.: school M.O. and assistant M.O., Southend-on-Sea.
HILLENBRAND, F. K. M., M.D. Rostock, D.C.H.: medical superintendent, Dr. Barnardo's Village Homes, Barkingside, Essex.
HOWELL-JONES, HUGH, M.R.C.S., F.F.A.R.C.S., D.A.: honorary anæsthetist, Italian Hospital, London.
LEWIS, E. G., M.B. W'rand: assistant M.O., Folkestone area, Kent.
STIRK, D. I., F.R.C.S.: consultant surgeon, Exeter clinical area, and with duties in North Devon.

Birmingham Regional Hospital Board:

BOYD, W. N., M.B. Glasg., F.R.C.S.E., D.M.R.D.: part-time consultant radiologist, Stoke-on-Trent group of hospitals.
LITCHFIELD, J. A., M.D. Birm., M.R.C.P.: part-time consultant physician (geriatrics), Mid-Worcestershire group of hospitals.
PILKINGTON, T. L., M.R.C.S., D.P.M.: consultant psychiatrist and deputy medical superintendent, Lea Colony, Bromsgrove, and Lea Castle Colony, Kidderminster.
SHINTON, N. K., M.B. Birm., M.R.C.P.: consultant pathologist, Coventry group of hospitals.

East Anglian Regional Hospital Board:

BASU MALLIK, M. K., M.B. Calcutta, B. OBST.: registrar in obstetrics and gynæcology, Peterborough group of hospitals.
DOWNES, MARGARET M., M.B. St. And., M.R.C.O.G.: part-time consultant obstetrician and gynæcologist, Lowestoft and Great Yarmouth hospitals.
GRIFFITHS, SHEILA M., M.B. Lond., registrar in geriatrics, Ipswich and East Suffolk hospital group.
HAND, B. H., M.S. Lond., F.R.C.S.: consultant surgeon, Ipswich and East Suffolk Hospital.
HUGHES, J. P., M.B. Lond., M.R.C.P.: senior medical registrar, Ipswich and Easy Suffolk Hospital.
HUSAIN, F., M.B. Karachi: anæsthetic registrar, Ipswich and East Suffolk Hospital.
JAFRI, M. A., M.B. Punjab, D.T.M. & H.: medical registrar, Peterborough hospital group.
KUMAR, S. P., M.B. Patna, D.O.M.S., D.O.: ophthalmic registrar, Norfolk and Norwich Hospital.
LUDBROOK, JOHN, M.B. N.Z., F.R.C.S.: surgical registrar, Norfolk and Norwich Hospital.
MEHTA, M. D., M.B. Lond., F.F.A. R.C.S., D.A.: consultant anæsthetist, King's Lynn area hospitals.
MUNRO, I. B., F.R.F.P.S., M.R.C.P.: senior medical registrar, United Norwich Hospitals.
SLADE, P. R. H., CH.M. Brist., F.R.C.S.: senior registrar in thoracic surgery, Papworth Hospital.
SYKES, W. S., B.M. Oxon.: anæsthetic registrar, Ipswich Hospital.
WALKER, A. R., M.B. Lond.: registrar in psychiatry, St. Andrew's Hospital, Thorpe.
YEALLAND, M. F. T., M.B. Cantab., M.R.C.P.: consultant neurologist, United Cambridge Hospitals and Regional Board hospitals.

Obituary

JAMES WILLIAM BROWN

M.D. Lond., F.R.C.P.

Dr. Brown was one of the most colourful and original personalities of the Sheffield Medical School, yet he had achieved much of his reputation before he became regional cardiologist in 1952. During his years in Grimsby as a general practitioner and later as a consultant his keen interest in congenital heart-disease enabled him to build up a remarkable knowledge of this particular facet of cardiology. No baby with a congenital heart disorder was born or died within miles of Grimsby but that he knew of the patient. This exceptionally wide experience was the foundation of his book, *Congenital Heart Disease*, which was published in 1939.

He was born in Gloucester in 1897, and after serving with the French Red Cross in the 1914–18 war he began to study medicine at the Middlesex Hospital and qualified in 1923. He settled in practice at Cleethorpes the following year and moved to Grimsby in 1931. In 1938 he gave up his general practice to devote all his time to cardiology, and he became cardiologist to the Grimsby and Scunthorpe Hospitals and to the Lincoln County Hospital.

When Dr. Brown became cardiologist to the Sheffield region in 1952 he was also appointed a part-time lecturer and clinical teacher of the University. Of his work there C. H. S.-H. writes:

"With the move to Sheffield, Brown took on the onerous task of building up a department and of using the most advanced techniques available for the investigation of cardiac cases. His success was largely due to his single-mindedness and to his capacity to win the loyalty of his juniors. An impressive flow of publications has resulted from the few years spared him, and he had already begun to prepare for the task of delivering the St. Cyres lecture due in 1959 when his illness overtook him. He was a man of rugged individualism such as is peculiarly characteristic of our profession. He was a delightful colleague, a teacher with a fund of humour and stories, and one whose care for the welfare of his assistants knew no bounds. His clinical experience and wisdom will be missed by patients and students alike."

D. C. M., who knew Brown through all his professional career from their student days together at the Middlesex Hospital, describes their friendship as "a very rewarding experience".

"Brown was," he writes, "a tireless and indefatigable worker. His widely scattered clinics entailed a tremendous weekly mileage, but this was work that he loved and enjoyed. It was a pleasure to see him calm a refractory child, often with the help of a rabbit drawn in ink on an arm or a leg. He had a wide knowledge of medical literature, and gathered in his time a library of selected works of great importance—including many rare and valuable editions. One of his abiding hobbies was hunting through antique shops; and great was his pleasure in finding something of interest—particularly a piece of china, such as a Meissen plate. A great naturalist, with a fine knowledge of botany, he loved the countryside, and rarely was his fishing-rod absent from the back of his car."

FREDERICK ELLIOTT

T.D., M.B. Durh.

Dr. Elliott, a medical officer of the Home Office and a former medical officer of the Ministry of Pensions, died on Aug. 29 at his home at East Sheen at the age of 47.

He was born in Sunderland and was educated at the Royal Grammar School, Newcastle upon Tyne, and at the medical school of the University of Durham. After qualifying in 1936, he held resident posts in Newcastle hospitals. It was his original intention to enter general practice, but before doing so he wished to see something of conditions overseas, and he joined the Blue Funnel Line as ship's surgeon, completing several voyages to the Middle and Far East. His plans to settle in general practice were interrupted by the war, during which he served with the R.A.M.C. in the Western Desert, Persia, Iraq, and Sicily. In 1944 he was severely wounded, and spent over a year in hospital before he was discharged in 1945 as medically unfit for further service, his right leg having been amputated below the knee, and his left knee-joint ankylosed. Some months later he joined the staff of the Ministry of Pensions as a limb-fitting surgeon at Roehampton, where his specialised knowledge of artificial limbs was of great value to his patients. He contributed the chapter on the loss of a leg to our *Disabilities* series (*Lancet*, 1948, ii, 744). In 1949 he joined the Home Office as an established medical officer.

P. L. C. C. writes:

"Elliott's cheerful acceptance of his physical disability endeared him to all who knew him. Possessing a keen sense of responsibility, he brought to his work not only high professional capability, but a quality of understanding and tact which was impressive. It will not surprise his many friends that in his last illness he faced with great fortitude and patience what his own medical knowledge must have told him from the onset was a hopeless prognosis."

Dr. Elliott married Miss Joan Bullen in 1939. She survives him with a daughter.

Diary of the Week

OCT. 5 TO 11

Sunday, 5th

UNIVERSITY COLLEGE HOSPITAL, London, W.C.1
10.15 A.M. Prof. C. E. Dent: Dwarfism.

Monday, 6th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. A. J. Quick (Marquette University): Hereditary Hæmorrhagic Diseases, Their Classification and Diagnosis.
INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1
5.30 P.M. Dr. Derek Richter: Protein Metabolism of the Brain.

Tuesday, 7th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5.15 P.M. Mr. W. J. Dempster: Kidney Transplantation.
6.30 P.M. Mr. Arnold Gourevitch: Intestinal Obstruction in the Newborn.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Physical Medicine, Orthopædics.* Dr. D. A. Brewerton, Mr. Ronald Furlong, Mr. O. J. Vaughan-Jackson: Management of Deformities of the Rheumatoid Hand.
KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark Hill, S.E.5
4.45 P.M. Mr. H. J. Seddon: Recent Work on Poliomyelitis. (Thomas Percy Legg lecture.)
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. J. Hare: Keratinisation.

Wednesday, 8th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.15 P.M. Prof. A. W. Wilkinson: Water and Mineral Requirements after Operation.
6.30 P.M. Mr. A. H. M. Siddons: Bronchiectasis.
ROYAL SOCIETY OF MEDICINE
5 P.M. *Comparative Medicine.* Dr. F. O. MacCallum: Aspects of Immunity in Virus Diseases. (Presidential address.)
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Dr. E. A. Brown (Boston): Single Annual Emulsion Injection for Pollinosis.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Arthur Tickner: Fats and the Skin.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. F. P. Lee Lander: Lung Manifestations of General Diseases.
MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) *Pathology.* Dr. Hermann Lehmann: Abnormal Hæmoglobins.

Thursday, 9th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Mr. W. E. Tucker: Traumatic Syndrome Phases and Stages: Certain Injuries, their Prevention and Treatment. (Hunterian lecture.)
6.15 P.M. Mr. Dickson Wright: Exophthalmos.
ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology.* Prof. Norman Ashton, Dr. John Speakman (Toronto): Trabecular Structure in Relation to the Problem of Glaucoma.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8 P.M. (Clarendon Restaurant, Hammersmith, W.6.) Mr. Arnold Walker: Midwifery Before We Were Born. (Presidential address.)

Friday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.15 P.M. Mr. O. J. Vaughan-Jackson: Hand Infections.
6.30 P.M. Dr. A. C. Smith: Treatment of Tetanus.

Notes and News

MINISTER RECOGNISES HYPNOSIS AS ANÆSTHETIC

THE London Executive Council has agreed to pay a doctor a fee (£1 15*s.*) for the attendance of a second doctor to produce anæsthesia by hypnosis for the suture of the perineum in a maternity medical service case. When the claim was first referred to the Council in January, 1957, it held that it only had authority to pay such a fee when a second doctor "gave an anæsthetic", and that it had no specific authority to pay a fee when a second doctor was called to "provide hypnosis". But it advised the doctor to refer the matter to his local medical committee for its opinion. The committee, with the support of the General Medical Services Committee and the anæsthetists group committee of the British Medical Association, decided that hypnotism induced by a medical practitioner should be regarded as an anæsthetic. The claim was then referred to the Minister of Health, who on July 21 wrote:

"Provided the Local Medical Committee is satisfied that the medical practitioner who is called in to administer the anæsthetic is accustomed to use hypnosis as part of his professional practice, the Minister would have no objection to the payment of a fee as if an ordinary anæsthetic had been used."

University of London

On Aug. 6 the degree of M.D. was conferred on G. G. Meynell and Alexander Paton.

University of Liverpool

On Sept. 26 the degrees of M.B., CH.B. were conferred on Malvina Harris.

University of Durham

On Sept. 27 the D.P.M. was conferred on the following:

J. R. B. Ball, N. E. Crumpton, S. L. Davies, Arthur King, Peter Roughead.

Royal College of Obstetricians and Gynæcologists

At a meeting of council on Sept. 26, with Prof. A. M. Claye, the president, in the chair, the following were admitted to the membership:

Prabhavathy Aiman, Prasannatissa Harischandra Amarasinghe, D. T. C. Barber, C. T. H. Barrett, W. P. Bonnici, John Breeze, J. M. Brudenell, D. Pui-Chee Chan, H. J. H. Claassens, C. J. T. Craig, Dilip Ranjan Das, R. M. Davie, R. F. Drake, G. R. Duncan, Diana Edwards, G. H. Ellidge, Wellege Hemachandra Fernando, L. H. Fienberg, J. MacD. G. Harley, Denys Heginbotham, J. B. Hemsley, Alice Hsiang-Lien Hsu, T. R. Hunt, P. J. Huntingford, Sylvia R. Ingold, Katherine I. Jack, R. D. Johnstone, E. W. P. Jones, A. J. Keane, A. C. Keast, D. M. D. King, Sybil V. Kinley, Daphne R. Lowe, John McGlone, Sheila Malhotra, D. T. Mathews, C. C. Mitra, W. P. L. Morrison, A. D. Muirhead, Salvino Muscat, Isabella R. Napier, Hannah J. Pash, J. H. Peters, D. W. Pfanner, D. M. Reader, W. J. C. Rebello, John St. George, P. C. Stichbury, J. O. Struthers, W. M. E. Tweed, Radha Naravan Udipi, Thiagarajah Visvanathan, A. W. G. Weir, Dorothy J. Whitney, W. G. Wicks, Balasubramaniam Yoganathan.

At a meeting on Sept. 27 Prof. G. Shedden Adam, of Brisbane, was appointed Bernhard Baron travelling scholar for 1959.

Ciba Awards

The Ciba Foundation is offering awards for experimental research into problems of ageing. The closing date for applications is Jan. 10, and further information may be had from the Foundation, 41, Portland Place, London, W.1.

Lebanon Hospital for Mental and Nervous Disorders

The annual meeting of this hospital will be held in the Cora Hotel, Upper Woburn Place, London, W.C.1, on Wednesday, Oct. 22, at 5 P.M. The speakers will include Dr. H. J. Eustace. Further particulars may be had from the London Office, Drayton House, Gordon Street, W.C.1.

Royal Anthropological Institute of Great Britain and Ireland

On Thursday, Oct. 16, at the Institute, 21, Bedford Square, London, W.C.1, Dr. Hermann Lehmann will give a lecture on abnormal hæmoglobins. On Friday, Nov. 28, at the Royal Society, Burlington House, W.1, Sir Wilfrid le Gros Clark will give the Huxley lecture on Bones of Contention. Both lectures will be held at 5.30 P.M.

Postgraduate Travelling Fellowships

These fellowships, which the Postgraduate Medical Federation is offering to doctors and dentists, are available in clinical as well as in preclinical branches of medicine, surgery, or dentistry. We regret that owing to our error reference to clinical branches was omitted from the advertisement which appeared on Sept. 20. Full particulars will be found in a corrected announcement in our advertisement columns this week.

Association of Surgeons of Great Britain and Ireland

The annual meeting of this Association will be held in London from April 23 to 25. Further particulars may be had from the hon. secretary of the Association, 47, Lincoln's Inn Fields, W.C.2.

London Jewish Hospital Medical Society

On Thursday, Oct. 9, at 8.15 P.M., at 11, Chandos Street, W.1, Mr. I. Preiskel will give his presidential address to this society. He will speak on some milestones in the progress of surgery.

Asian-Pacific Congress of Cardiology

This congress will be held in Melbourne during the last week of May, 1960. Further particulars may be had from the hon. secretary, Dr. A. E. Doyle, Alfred Hospital, Melbourne, S.1, Victoria, Australia.

Mr. Griffith Evans, F.R.C.S., will give four lectures on basic science and Christian healing at Charing Cross Chapel, London, W.C.2, at 7 P.M. on Tuesdays, Oct. 7, 21, 28, and Nov. 4.

On Monday, Oct. 20, at 3 P.M., at the University Union, the Bishop of Bradford will give the inaugural address to the faculty of medicine of the University of Leeds. His subject will be the Wholeness of Man.

On the four Fridays of November, at 8 P.M., lectures on spiritual healing will be given at St. Mark's Church, Hamilton Terrace, London, N.W.8, and on Nov. 21 the speaker will be Dr. Desmond O'Neill.

The Bristol Young Doctors Group, which was formed earlier this year, will hold a meeting on Monday, Oct. 13, in the board room of Bristol Royal Infirmary at 8 P.M., when there will be a discussion on the G.P. trainee scheme. The hon. secretary of the group is Dr. Derek Zutshi, P Block, Southmead Hospital, Bristol.

A meeting of the medical advisory panel of the London Amateur Boxing Association will be held at 25, Savile Row, W.1, on Wednesday, Oct. 22, at 8 P.M. A film of the Olympic Games boxing will be shown. Further particulars may be had from Dr. J. L. Blonstein, 69, Victoria Street, S.W.1.

Mr. R. B. Duthie has been appointed professor of orthopædic surgery and orthopædic surgeon-in-chief at the University of Rochester School of Medicine and Dentistry, Rochester, N.Y., U.S.A.

The Ministry of Pensions and National Insurance has produced *Notes on Overlapping Benefits, Allowances, and Pensions*, which includes a section describing the effect of a stay in hospital on a patient's entitlement to National Insurance benefits. Copies of the booklet may be had from the information division of the Ministry, 10, John Adam Street, London, W.C.2.

The council of the Institution of Electrical Engineers have set up a medical electronics discussion group. Further particulars can be had from the secretary of the institution, Savoy Place, London, W.C.2.

The annual students' dinner of Middlesex Hospital Medical School will be held at the Savoy Hotel, Strand, London, W.C.2, today, Friday, Oct. 3, at 7.30 P.M. Mr. Philip Wiles will be in the chair.

The United Hospitals' Choir are to give a concert in aid of the Imperial Cancer Research Fund on Tuesday, Nov. 25, in Chelsea Town Hall. Tickets (3*s.* 6*d.*, 5*s.*, 7*s.* 6*d.*) may be had from Miss E. Sorensen, South Western Hospital, Landor Road, Stockwell, London, S.W.9.

Births, Marriages, and Deaths

DEATH

LANDOR.—On Sept. 12, at Woollahra, New South Wales, Joseph Victor Landor, M.D., M.R.C.P., D.P.H., D.T.M. & H.